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OXYGEN IN THE TREATMENT OF LOBAR PNEUMONIA

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IN PNEUMONIA there is often a sufficient degree of anoxia to be definitely detrimental to the patient. This may be a factor of sufficient importance to decide the issue between recovery and death. The administration of oxygen will often completely relieve this anoxia. One must therefore consider the use of oxygen in this disease as an accessory method of treatment which, in the severer cases, may be indispensable.

Anoxia in pneumonia is of the arterial anoxemic type; that is to say, it is due to interference with the passage of oxygen into the blood, so that the fact of a decreased oxygen supply to the tissues is due to a desaturation of the hemoglobin. This is the type of anoxia in which the inhalation of oxygen-rich air is effective — as opposed to anemic anoxia, in which the oxygen-carrying power of the blood is diminished, and to stagnant anoxia, in which the velocity of capillary flow is decreased. Anoxemia in pneumonia may be the result of three main factors, or more usually a combination of the three. It may result from an insufficient amount of oxygen entering the alveoli because of shallow breathing due to acute pleurisy. It may also be due to a partial shunting of unoxygenated blood through a lobe in the stage of early or red hepatization, when exudate in the alveoli prevents the entrance of air but circulation through the affected lobe is still maintained. Of course oxygen is effective only in so far as it can reach the unsaturated hemoglobin, and in cases where air is completely excluded from lung tissue, through which blood still flows, increased oxygen tension in the air is of no value. But it is probable that such a shunting is not often a dominant factor, and when it does occur oxygen-rich air certainly can aid in controlling the general desaturation that results from the dilution of the unoxygenated blood which has passed through the affected lobe into the rest of the patient's general circulation. The third and principal cause of the anoxemia in pneumonia is probably widespread congestion and edema, which make the lumens of the bronchioles smaller and the alveolar walls less permeable. In such cases an increased tension of oxygen in the air that gets into the alveoli means an increase in hemoglobin saturation and a decrease in anoxia. It is in the severe and late cases, and especially in those in which there is a spread of the pneumonia to several lobes or an added factor of cardiac weakness, that oxygen is of the greatest value.

I propose to present a brief summary of the effects of anoxia in pneumonia, and to consider the main indications for oxygen therapy and the simpler and more effective methods of carrying it out. While I shall speak of the clinical results of this treatment in general, I shall make no attempt to present any statistical evidence as to the value of oxygen in pneumonia. Stadie,[1] in 1922, in emphasizing the value of this type of therapy, pointed out that it did not lend itself to statistical analysis. At the present time, when both adequate serum therapy and sulfapyridine are proving their worth in such spectacular fashion, it is quite impossible to determine the value of an accessory factor such as oxygen by any study of mortality figures. It is my purpose, also, to mention very briefly the use of high concentrations of oxygen in the treatment of abdominal distention, which is such an appalling complication of some cases of pneumonia.

That marked arterial unsaturation exists in many cases of pneumonia was demonstrated as early as 1912 by Hurter. This anoxemia has been shown to be as great as that which, when brought about experimentally, produced severe symptoms. Its action on the nervous and circulatory systems is of particular importance. Anoxia occurring in pneu-

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monia affects the nervous system by producing symptoms the most prominent of which are headache, neuromuscular weakness and delirium. It is well to remember that in very toxic patients such symptoms are often due not to the toxemia but to the anoxia, and therefore may be preventable or correctable by oxygen. The effects on the circulatory system are equally important. As Meakins,[2] Long and Evans[3] and others have pointed out, reduction of oxygen supply is the only factor that can be shown definitely to reduce cardiac glycogen and thus to reduce the efficiency of the heart. In elderly patients, especially, this is of significance in pneumonia. Clinically, anoxia is ordinarily seen to produce tachycardia, and it is usually observed that oxygen which causes cyanosis to disappear in pneumonia also reduces the pulse rate. Other effects of anoxia which are of importance in pneumonia are nausea and vomiting, and an increase in the rate, and to a less extent in the depth, of respiration.

The best clinical gauge of the extent of the anoxia in pneumonia is the degree of cyanosis. Roughly speaking, cyanosis that is just recognizable means a desaturation of about 10 per cent; that is, the normal saturation of 95 per cent has been reduced to 85 per cent. If cyanosis is very marked it may mean a desaturation below 70 per cent. Cyanosis, then, may be considered the cardinal indication for oxygen therapy. Dyspnea, however, also may be considered an indication if it is marked. Barach and Levy[4] have called attention to the fact that in heart disease a potential anoxia may be present, but that by extra respiratory effort actual anoxia may be prevented. Such effort is exhausting and an extra load on the heart. In pneumonia, I believe, the same situation exists, and if dyspnea is severe, even without cyanosis, an attempt to relieve it by oxygen should be made.

Any method that sufficiently increases the oxygen tension in the inspired air and is not too disturbing to the patient is adequate. So far as I know, no method of giving oxygen intravenously over a long period that is practical or safe has been developed. Subcutaneous oxygen was studied a few years ago in our clinic, and appeared to be quite ineffective in relieving anoxia clinically or in decreasing the desaturation of the blood. This method has recently been studied experimentally by Barker and his associates,[5] who reached the same conclusion. Among the methods of giving oxygen by inhalation I shall consider three: masks or face inhalers, nasal or oropharyngeal insufflation and the open box. Oxygen of course may be given effectively by one of the large tents or by placing the patient in an oxygen room. Such methods are excellent, but the equipment is so expensive that in a general hospital it is usually impossible to maintain enough of it to serve the many patients who need oxygen.

Masks or facial inhalers of various sorts have been employed for many years, and some have proved fairly efficient. The B.L.B. mask, oronasal type, which has been recently developed at the Mayo Clinic by Boothby, Lovelace and Bulbulian,[6] has seemed to me by far the best yet devised.* Recent tests that I have made have convinced me that this apparatus is very efficient, and many patients tolerate it very well. Furthermore, it is less wasteful of oxygen than are most of the other methods.

In utilizing the nasal catheter I have for years employed the method of oropharyngeal insufflation of Wineland and Waters.[7] I have followed their technic carefully and have found the method usually well tolerated by most adults. The studies of Barker, Parker and Wassell on the alveolar air in patients treated by this method have shown that in order to obtain a therapeutically effective concentration, a flow of at least 4.5 to 6 liters per minute must be maintained; in some cases this must be increased to 8 or 10 liters. I have thought that in general this method was the best for the average adult, but if the need for oxygen is great the open box or the B.L.B. mask should be used. While the testing of the latter apparatus is not yet by any means completed, I have gained the impression that it is even slightly more efficient as to the delivery of oxygen than is stated by its originators.

The open-box method[8] is the one of choice for infants and children. It is also effective in adults, and in my clinic is employed in those cases in which a higher concentration of oxygen is needed than can be easily obtained by the nasal catheter. In the future it is probable that many such cases can be better treated by the B.L.B. mask. In most of the adult cases of pneumonia, however, oropharyngeal insufflation has been found satisfactory. In using the open box or any tent, it is of particular importance, as Barach and Levy[4] have emphasized, to know exactly what the patient is getting, and tests of the oxygen content of the air in the apparatus should be routinely carried out at regular intervals. Many of the disappointing results of oxygen therapy are due to improper application of apparatus.

A review of the last 300 cases (up to February, 1939) diagnosed as lobar pneumonia at the Rhode Island Hospital shows that 142 patients (47 per cent) received oxygen at some time during the course of the disease. Of the patients treated with

*It is to be noted that the oronasal and not the nasal type of B.L.B. mask should be used, as one cannot trust a sick patient not to breathe through the mouth.

oxygen, 90 received it by the open-box method, and 52 by the catheter method. Most of those on whom the open box was used were children, and all those who received oxygen by nasal catheter were adults. The open box was, however, of great value in a few of the more desperate cases in adults in whom treatment by nasal catheter seemed inadequate.

A further use of oxygen in pneumonia, fortunately a rather rare one, remains to be mentioned, namely high concentrations for the relief of abdominal distention, as suggested by Fine and his associates.[9] I[10] have described a modification of the box method by which 98 per cent oxygen can conveniently be given, and recently Congdon and I[11] have reported the clinical results in 40 cases treated by this means. Although severe distention usually, in our experience, can be relieved by ordinary means, — enemas and peristaltic stimulants, — we think that occasionally, when such means have failed, high oxygen concentrations may be life-saving.

Summary

In the treatment of lobar pneumonia, oxygen therapy is an accessory method of considerable value that is occasionally indispensable. Its value lies in the relief of the deleterious effects of anoxia, especially on the nervous and circulatory systems.

Cyanosis is the best clinical sign in determining the presence and degree of the anoxia in pneumonia, but severe dyspnea, even without cyanosis, is also an indication for the use of oxygen.

The most practical and inexpensive methods for giving oxygen are oropharyngeal insufflation through a nasal catheter, and the open box. To these must now be added the new B.L.B. mask, which appears to give very excellent results.

At the Rhode Island Hospital during the last three years almost 50 per cent of all patients with the diagnosis of lobar pneumonia have received oxygen either by nasal catheter or by open box. In the rare cases in which marked abdominal distention occurs, unrelieved by ordinary measures, 95 to 98 per cent oxygen given by the closed-box technic may relieve the situation.

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ATYPICAL BRONCHOPNEUMONIA OF UNKNOWN ETIOLOGY*

Possibly Due To a Filterable Virus

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DURING the academic year 1936-1937 the physicians associated with the Department of Hygiene of Harvard University observed a mild form of pneumonia which differed strikingly from pneumococcal lobar pneumonia and likewise from the usual types of bronchopneumonia. We had seen a few cases during the previous academic year that probably belonged in the same category. In the following college year the incidence of such cases increased, and during the fall and winter of 1938-1939 we saw a still larger number (Table 1).‡ Bock[1] has called attention to this in his account of our experience with acute infections of the upper respiratory tract in 1938. There has been considerable speculation as to whether this form of pneumonia constitutes a separate disease entity, and also as to its etiology. It has been referred to as "virus pneumonia" and as "acute interstitial pneumonitis." We have chosen to use the term "atypical bronchopneumonia."

TABLE 1. *Cases of Atypical Bronchopneumonia Treated at Stillman Infirmary during the Academic Years 1935–1936 through 1938–1939.*

Academic Year	Month										Totals
	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June	
1935–1936	0	1	0	0	0	1	1	1	1	0	5
1936–1937	1	2	3	8	5	3	0	0	1	2	25
1937–1938	0	2	9	0	6	0	8	5	4	1	35
1938–1939	4	12	20	19	12	3	6	5	—	—	81

A number of reports describing an atypical pneu-

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‡Besides the 81 cases cared for at the Stillman Infirmary, we have also had reports of 39 cases occurring among students who were treated by their family physicians.

monia or pneumonitis have appeared in the literature. Most of the descriptions are quite similar to our own observations, but the cases described by Cass[2] and Reimann[3] differed in some respects. The patients reported by Cass had marked prostration at the beginning of the illness, rather early appearance of the physical signs and a true leukopenia. Those reported by Reimann were very severely ill and seemed to have had a much more virulent infection than the ones we have seen. Those reported by Gallagher,[4] Bowen,[5] Allen[6] and Smiley et al.[7] and the group we have observed are strikingly similar. It is interesting that Stansfield[8] in 1923 published some observations on a series of patients who had an infection closely resembling the one we are describing.

In an attempt to describe the clinical picture we have reviewed the histories of 132 cases, all of which were treated in the Stillman Infirmary of Harvard University during the last four years.

Clinical Picture

The illness usually starts as a mild acute infection, resembling "grippe," in which symptoms referable to the respiratory tract are mild or absent. The patient does not have the appearance of one who is developing a pneumonic process. The usual story is that during the preceding day or two he has had some headache, malaise, a little fever and perhaps mild chilly feelings, together with peripheral aches and pains. He may have had a slight cough, but this is frequently so mild that it is not mentioned by the patient unless he is questioned on the point. There is generally little sputum and no history of chest pain.

The physical examination reveals little except slight reddening of the pharynx and an elevated temperature. The pulse is not particularly elevated and the respiratory rate is normal. The diagnosis is usually made by x-ray on the third or fourth day, when a patch of hazy dullness is found in one lung field. It is well to remember that even at this stage there are no abnormal physical signs to be found on examination of the chest. There is some cough and perhaps a small amount of mucopurulent sputum. The sputum is not bloody or rusty.

The temperature returns to normal by the sixth or seventh day, and by this time coarse rales may be heard over a localized area. The patient remains in bed another week, is gradually allowed to resume activity, and at the end of another week to ten days has returned to a normal state of well-being.

A review of the details of the histories of these patients reveals that less than half of them had had a cold or other respiratory infection during the previous three weeks (Table 2). About one quarter of them had had a relatively sudden onset, feeling moderately ill in the course of twenty-four hours or less. The explosive onset seen in lobar pneumonia did not occur. The remainder gave a story of the gradual development of symptoms over the course of two or three days. Occasionally the patient had been sick for a week or more with what he considered "grippe" or a bad cold, and had either been taking care of himself in his room or going to classes. He showed evidence of either a fully developed or resolving pneumonic process when first seen. This occurred in 6 cases. Almost all the patients developed a slight cough within the first few days. Headache, which might be severe, was very common; it was frequently frontal and occasionally unilateral. Some degree of peripheral aches and pains was present quite frequently, with a few cases of marked lumbar pain. Aching in or about the eyeballs was quite marked in several cases. Mild sore throat was relatively common and coryza might be present, but this was infrequent. Some patients complained of a slight tightness of the chest or substernal discomfort, but any degree of real chest pain was exceptional. Only a few experienced a shaking chill, although chilly feelings or chilliness occurred rather frequently. A small number had gastrointestinal symptoms at the beginning: nausea and vomiting, or diarrhea. Sweating was frequently present at the onset and sometimes became marked later in the illness. Prostration was occasionally present to some degree, but in general the picture was that of a mild infection.

Table 2. *Onset, Preceding History and Presenting Symptoms in 132 Cases.*

Clinical Factor	No. of Cases
Onset:	
Sudden (24 hours)	35
Gradual (several days)	97
History of preceding cold	54
No cold within previous 3 weeks	78
Symptoms:	
Cough	111
Headache	70
Aches and pains	70
Malaise	56
Chill	17
Chilliness	51
Sputum at onset	43
Sore throat:	
Mild	43
Marked	7
Coryza	27
Chest pain, moderate	4
Substernal discomfort or "tightness"	20
Nausea and vomiting	3
Diarrhea	1
Nausea, vomiting and diarrhea	1

The initial physical examination was noteworthy because so regularly normal. A temperature of 100 to 101°F. and a little pharyngeal red-

dening were the only frequent positive findings. A tinge of cyanosis was observed in only a few cases. Respiratory distress was absent and examination of the chest was normal. The abdomen was soft and flat. A palpable spleen was noted in a few cases.

The course of the disease was variable. In a small number of cases the temperature dropped to normal in the first twenty-four to forty-eight hours after the patient went to bed, and remained normal thereafter. Sometimes the temperature fluctuated irregularly, rising as high as 104 or 105°F., but usually covering a range of 101 to 103 and remaining elevated for five to seven days. The pulse rate was low in proportion to the fever, and was frequently a very reassuring sign in the few patients who appeared to be seriously ill. The respirations were almost never significantly increased. This was one of the most constant findings in these cases. During the earlier part of the febrile period considerable headache with some malaise and sweating was present, and later intermittent bouts of cough with varying amounts of sputum were common. The patient's subjective discomfort, however, was less than one might expect on casual inspection of the temperature chart and x-ray film.

In a little more than half the cases physical examination of the chest revealed dullness on percussion. This usually appeared on the second to the fifth day and was frequently barely detectable. Marked widespread dullness appeared in only a small proportion of the cases. Breath sounds were normal at the beginning, but tended to become diminished with the progress of the disease and in some cases were almost suppressed. Some degree of diminution of breath sounds was found in a majority of the cases, but any marked bronchovesicular or frank bronchial breathing was uncommon. The development of bronchial breathing sometime in the course of the illness was observed in only 15 per cent of the cases, and when present often disappeared in twenty-four to forty-eight hours. Significant alterations of the tactile fremitus and marked changes in the whispered and spoken voice were likewise found only occasionally. Rales were late in appearing, not being heard until the fifth, sixth or seventh day in bed, and sometimes not until the eighth to twelfth day. The rales were coarse and were apt to persist for one or two weeks before completely clearing. A small proportion of the cases never developed any abnormal physical signs.

Although in most cases the sputum was very scanty throughout the course of the illness, the production of profuse, mucopurulent sputum occurred occasionally. No significant degree of tympanites was encountered in any of the patients. Nervous symptoms, such as those described by Reimann,[3] we have not seen at all. In a few cases there was extension of the process to another lobe, but this was exceptional.

The average duration of infirmary care was ten to fourteen days. Several patients had a rather desultory, lethargic course with prostration and ran a low-grade fever for two or three weeks. These required a prolonged convalescence. Severe reactions with great prostration, prolonged high fever or the appearance of critical illness were rare.

The following abstracts are illustrative of typical cases:

Case 1. E. P., a college student, aged 21, was admitted to the Stillman Infirmary on November 23, 1938. He had had a "cold" beginning 2 days previous to admission. The day before entry he had had chilly feelings, a sensation of tightness under the sternum and a dry hacking

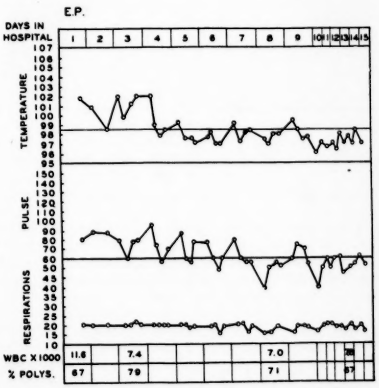

Chart 1.

cough. He had some headache, fatigue and mild malaise when first seen. He had had no sore throat, chest pain or sputum, and he did not feel particularly ill. On admission the temperature was 102°F., the pulse 80, and the respirations 20 (Chart 1).

Physical examination revealed a young man sitting up in bed in no particular discomfort other than an occasional cough. The skin was warm and moist. There was no adenopathy. The nose and throat were essentially normal, and examination of the chest was negative. The rest of the physical examination was essentially normal. An x-ray film of the chest taken on the 3rd hospital day revealed an area of soft, hazy density at the right base occupying the cardiac angle (Fig. 1).

On the 3rd and 4th hospital days the patient had rather severe headache, perspired freely and felt moderately sick. His cough was more marked and he was producing small amounts of mucopurulent sputum, which was

not bloody. On the 5th day slight dullness to percussion and a moderate number of coarse, moist rales were found at the right lung base posteriorly. At this time the temperature dropped to normal, the headache had subsided and the patient felt very much improved. Thereafter he made steady improvement and had an uneventful recovery. The dullness disappeared after a few days, but coarse, moist rales persisted until the 12th day. The patient was

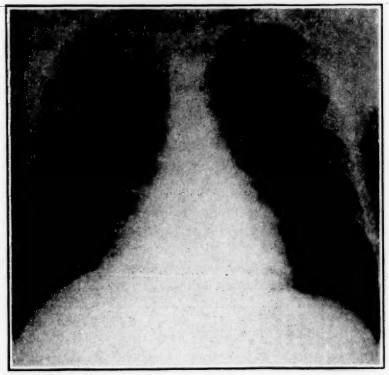

FIGURE 1. *Case 1.*
This chest film was taken on the third hospital day.

discharged on the 15th day and returned to his classes 1 week later.

The sputum contained pneumococcus, Type 6. There were no complications.

Comment. This patient represents a fairly typical mild case. The lesion occupying the cardiophrenic angle was a very common finding in such cases.

CASE 2. P. S., a college student, aged 20, was admitted to the Stillman Infirmary on November 28, 1938. Ten days previously he had had some coryza and sore throat. This had subsided, but for the week preceding admission he had had some cough without expectoration. For the previous 3 days he had felt that he had some fever but very little malaise.

The day of admission the temperature was 100°F., the pulse 80, and the respirations 20 (Chart 2). Physical examination revealed a young man who was coughing but who did not appear to be very ill. A few fine rales were heard at the base of the right lung, but there were no other abnormal physical signs.

The temperature rose to 102°F. the day after admission and the patient felt moderately ill. At that time some dullness to percussion and diminution of breath sounds were found at the right lung base. An x-ray film revealed a large area of density extending upward and downward from the right hilus along the right border of the heart (Fig. 2). By the 3rd day the patient felt very much improved, and except for some persistence of the cough had very few symptoms thereafter. He continued to have an irregular temperature up to 101°F., but this had returned to normal by the 6th day. Numerous medium and coarse, moist rales appeared in the right lower chest, and a small number were also heard in the left lower chest. The rales persisted until the 12th day. The patient was

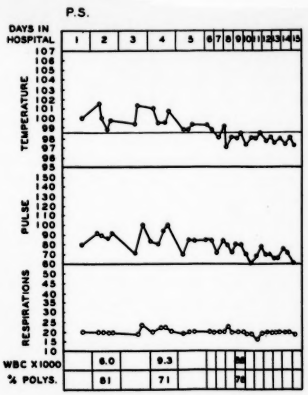

CHART 2.

discharged on the 15th day to continue convalescence with relatives.

No pneumococci were found in the sputum. There

FIGURE 2. *Case 2.*
This chest film was taken on the second hospital day.

was an uneventful recovery without any complications.

Comment. This patient also is an example of a fairly typical mild infection. The pulmonary lesion presumably began several days before the patient went to bed. The x-ray film illustrates the fan proceeding from the hilus, which has been described by others.

CASE 3. G. M., a law student, aged 22, entered the Stillman Infirmary on September 27, 1938. He had felt well up to the previous day, when he had suddenly begun to have aches and pains in his muscles and all over his body, developed some headache, and felt feverish. During the night he perspired freely and the next morning felt better. He went to his classes, but during the morning felt very sick with general malaise and fever.

At admission the patient felt moderately ill, but had no cough. The temperature was 101°F., the pulse 90, and the respirations 20 (Chart 3). The skin was hot and moist. The pharynx was moderately reddened. Examination of the chest was negative. The physical examination was otherwise essentially normal.

On the 2nd day the patient still had considerable headache and developed a little cough. An x-ray film showed an indefinite area of density extending down from the right hilus to the cardiophrenic angle. He continued to have an irregular temperature, up to 104°F., had considerable cough and headache, and perspired freely. On the 5th day some dullness to percussion and diminution of breath sounds were found over the right lower chest. A second x-ray film taken the same day showed considerable increase in the consolidation at the right lung base (Fig. 3). On this day the temperature dropped to normal. This was shortly followed by a chill and the temperature again rose to 103°F.

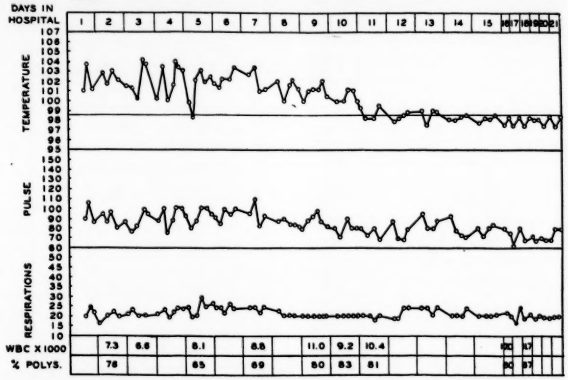

CHART 3.

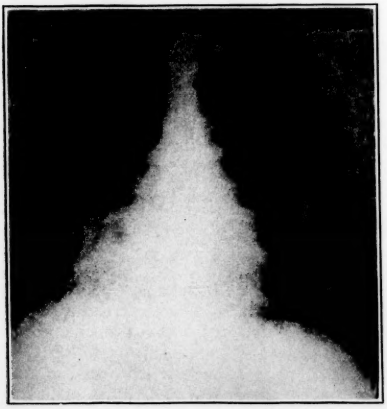

FIGURE 3. *Case 3.*
This chest film was taken on the fifth hospital day.

The patient continued to feel moderately ill, with profuse perspiration and severe headache. The cough persisted, and he raised moderate amounts of mucopurulent sputum, which on a few occasions was blood-streaked. Abnormal physical signs became more marked, and on the 7th day there was dullness posteriorly, extending downward from the angle of the scapula, with a moderate number of medium moist rales in that area. A third x-ray film taken on the 10th day showed a slight increase in the amount of density over the previous observation. The patient continued to have an irregular fever, which gradually subsided by lysis, reaching normal on the 12th day. Large numbers of medium and coarse, moist rales appeared throughout the entire right lower chest, persisting until the 19th day. There was no bronchial breathing at any time. The white-blood-cell count, which had been within normal limits, rose to 17,000 on the 16th day.

The patient was discharged on the 21st day to Lyman House for convalescence. He had lost 12 pounds and felt rather weak, but otherwise was symptom-free. He had an uneventful convalescence and no complications.

Repeated sputum examinations revealed no pneumococci.

Comment. This patient was moderately ill and probably had a spread of the process about the 5th day. The relatively low pulse and respiratory rates, the absence of

pneumococci in the sputum and the normal white-blood-cell counts, with a rise to 17,000 on the sixteenth day, are of interest.

CASE 4. R. H., a graduate student, aged 28, was admitted to the Stillman Infirmary on March 18, 1939. One month previously he had had an upper-respiratory infection and had been in bed for 1 week. However, he made a complete recovery and felt well until the day before admission. On that day he experienced a tight sensation in his chest. The following day he found that he had a fever and therefore came to the infirmary. He had mild coryza, considerable malaise and ached all over. He had no cough.

Physical examination revealed a man who looked sick. The temperature was 101°F., the pulse 75, and the respirations 20 (Chart 4). The skin was hot and dry. There was slight nasal discharge, the tongue was coated and dry, and the pharynx showed mild generalized reddening. A few small lymph nodes were palpable. Examination of the chest was negative.

On the 2nd day in bed the patient developed a slight, dry cough, had a chill, and the temperature rose to 104°F. He had no appetite and felt prostrated. An x-ray film of the chest taken on the 3rd day showed a small area of haziness at the right cardiophrenic angle. During the next 3 days he had some nausea, vomiting and diarrhea. On the 5th day, slight dullness and bronchovesicular breathing were heard over the right lower chest. The physical signs increased, with marked dullness all over the right lower chest, bronchial breathing and increased whisper. Tactile fremitus was equal on both sides.

The patient continued to have an irregular fever, ranging from 101 to 104°F., for 8 days. He was listless, apathetic and prostrated by the illness. X-ray films showed an increase in the consolidation, which occupied the position of the middle lobe and a portion of the lower lobe of the right lung (Fig. 4).

Repeated sputum examinations were negative for pneumococci and acid-fast bacilli. Sputum culture revealed many alpha hemolytic streptococci and small numbers of staphylococci and *Neisseria catarrhalis*. Two blood cultures were negative. A Widal test was negative. The white-blood-cell counts were consistently normal.

The patient was discharged April 8. There were no complications, but the convalescence was prolonged.

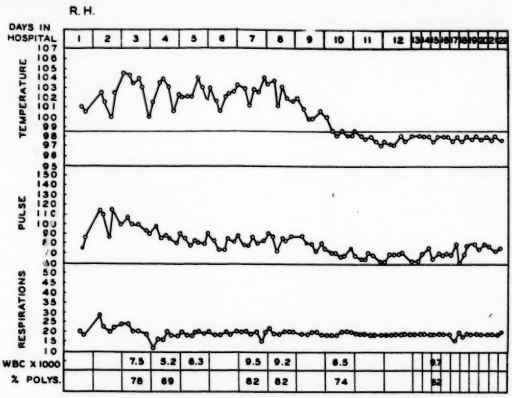

CHART 4.

Comment. This man felt and looked severely ill. The relatively slow pulse was reassuring, and the normal leukocyte count throughout the illness is of interest. Severe illness such as this case illustrates was seen rarely in this series.

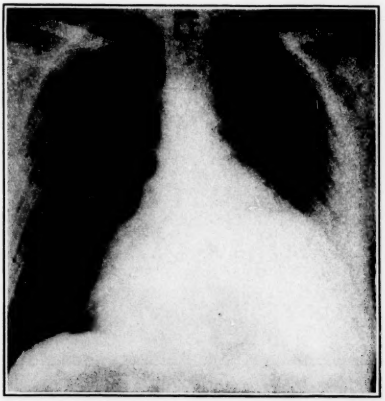

FIGURE 4. *Case 4.*

This chest film was taken on the fifth hospital day.

Roentgenological Observations

Since we frequently did not suspect a pulmonary lesion for several days, it has been difficult to determine accurately how soon x-ray changes can be detected after the illness begins. In a few cases where x-ray films were taken early, changes were found within twenty-four hours after the initial symptoms. Certainly x-ray changes are present for several days before abnormal physical signs can be detected. The roentgenogram usually discloses an area of hazy density extending out from the hilus region into the lower lung field, and occasionally into the midlung field. The margins of this area are ill defined, shading off gradually into the surrounding normal lung. As the disease progresses, the area increases in density, may increase in size and becomes more sharply defined. Resolution occurs as in other types of pneumonia, the density gradually diminishing and becoming more mottled and linear in type. A week to ten days after the peak of the illness the lung may show only a few linear bands of density in the previously involved area. The characteristic finding is lobular rather than lobar distribution of the lesion. Although a whole lobe was involved in a few cases, the majority showed only a section of one lobe to be affected. Basal lesions were commonest; upper lobe lesions were observed in only 9 cases. Lesions, usually termed central pneumonia, limited to the hilus region were found in 13 cases. More extensive shadows occupying the midlung field but not reaching the base were observed in 17 cases. The remaining lesions occupied either the right or left lower lung field, being found more frequently on the right. Bilateral lesions were observed in 13 cases. In the cases of patients who ran a mild clinical course it was quite common to find a small area of consolidation limited to one cardiophrenic angle. Evidence of consolidation and collapse were found in 7 cases.

Laboratory Data

The average case presented a normal or slightly elevated leukocyte count. Seventy-five per cent of the patients had an initial leukocyte count of 5000 to 12,000, the majority being from 7000 to 11,000. The percentage of polymorphonuclear cells was usually 70 to 75. Among those who had an initial leukocyte count higher than 12,000 were several patients with "walking pneumonia," several who had had an antecedent infection in the sinuses, pharynx or middle ear, and those who had been vomiting. In one third of the cases in which the initial leukocyte count was not over 12,000 there was a curious rise in the count during convalescence, occasionally reaching 17,000 to 20,000. While this might be taken to herald the onset of some complication, none appeared in this group. The percentage of polymorphonuclear cells found after the leukocyte count had risen was only slightly increased.

Through the facilities of the Massachusetts Department of Public Health we were able to have sputum examinations made on a large number of cases, but owing to several factors we were unable to carry out extensive bacteriological studies. Seventy sputum examinations were made in 53 cases, 41 of which were reported to contain no pneumococci and 29 to contain varying numbers of one or more type-specific pneumococci. No cases of Type 1 were reported, but 1 of Type 2 and 1 of Type 3 were found, and the remainder were scattered throughout the higher types — Types 4 to 32. Sputum cultures were done in a small group of these cases at the Massachusetts General Hospital, and a variety of organisms which can be found in any nonspecific respiratory-tract infection were reported.

In 11 cases* Enders, Sullivan, Hammon and Meakins,[9] of the Department of Bacteriology, Harvard Medical School, attempted to demonstrate an etiologic agent by the inoculation of a variety of laboratory animals, including mice, rabbits, guinea pigs, ferrets and *Macaca mulatta,* and of the chorioallantoic membrane of the hen's egg. The injection of blood, sputum and nasopharyngeal washings failed to induce in these species any recognizable pathologic changes.

Routine urine analyses were done on admission and at intervals throughout the infirmary stay. These were all negative except for occasional transient albuminuria and, very occasionally, small numbers of red blood cells in the centrifuged sediment.

Treatment

The basis of treatment has been the ordinary measures usually instituted in simple acute infections: bed rest, liberal fluids and normal diet, with added sodium chloride when there was any marked salt loss through perspiration. Codein has been used to help control cough, and the salicylates have been used to control the aching and malaise so common during the early part of the disease.

Oxygen therapy has not been necessary in any case; specific serum has not been used; sulfanilamide was used in 1 case without benefit, and sulfapyridine was not used.

Complications

One of the most striking features of the clinical picture was the absence of any serious complica-

*This group was made up of students at the Stillman Infirmary and nurses from a Boston hospital.

tions. In 1 case we had x-ray evidence of questionable fluid, but in no case did we note the occurrence of empyema. In 8 cases either marked follicular tonsillitis, acute sinusitis or otitis media was present when the patient was admitted to the infirmary, the pneumonic process either developing or being discovered subsequently. Sinusitis of moderate degree occurred in the course of the illness in 4 cases. Mild otitis media not requiring paracentesis occurred in 5. In 2 cases it was more severe, one requiring paracentesis and the other draining spontaneously. Mastoiditis did not occur. Urticaria occurred in 1 case. Ulcerations on the soft palate were observed in 1 case. In 1 case streptococcal pharyngitis with cervical adenitis occurred.

There were no deaths in this series.*

Epidemiology

During the academic year 1938–1939 a detailed follow-up study on 45 of the patients was carried out by Ernest B. Millard, Jr., and James H. Mithoefer,[10] students at the Harvard Medical School. They noted that the highest incidence of the pneumonia cases occurred in November and December, whereas the highest incidence of other respiratory infections occurred in February and March. This suggests that the illness in question is not etiologically related to the common cold. They were able to trace eight miniature epidemics in which exposure and contacts were studied carefully, and concluded that the infection is contagious, though not highly so, and is probably transmitted from one person to another by direct, casual contact. Because of the presence of multiple contacts, determination of an incubation period could not be carried out with any degree of certainty, but in four series of cases where multiple contacts were few, evidence was found to suggest an incubation period of seven to eleven days.

Summary

During the last four years a rather mild form of pneumonia has been observed among the students at Harvard University. During the academic year 1938–1939 it was much more prevalent, 81 cases having been cared for in the Stillman Infirmary and 39 cases reported by family physicians. The records of 132 infirmary patients have been studied with a view of describing the clinical course of the illness.

It began as a simple acute infection, with minimal respiratory symptoms, but usually with the early appearance of cough and later some degree of expectoration. The chill, chest pain, bloody sputum and prostration of pneumococcal lobar pneumonia were as a rule absent. A pulmonary lesion, most often beginning at the hilus and advancing outward toward the lateral chest wall or the diaphragm, was demonstrable early in the illness by x-ray examination. Physical signs were minimal, and absent altogether in certain cases. When present, they were late in appearing. Mild dullness to percussion, some diminution in breath sounds, followed by the appearance of coarse rales on the fifth, sixth or seventh day, were the usual findings. The course was ordinarily mild, with return of the temperature to normal in five to seven days. The pulse was only moderately accelerated, rarely rising above 90 or 100. The respiratory rate was almost invariably normal. Severe prostration was present in a few cases, but tympanites, delirium and other evidences of critical illness were not seen.

The leukocyte count was either normal or slightly elevated, with 70 to 75 per cent polymorphonuclear cells. In about one third of the cases there was a rise in the leukocytes during the latter part of the illness without the appearance of complications to explain it. Complications were few, and when present were mild. The more serious complications, such as empyema, lung abscess and bronchiectasis, did not occur. The majority of sputum specimens examined contained no pneumococci; somewhat less than half showed a pneumococcus, usually one of the higher types. Sputum cultures yielded a variety of organisms, and a small number of blood cultures were all negative. Attempts to isolate a filterable virus were unsuccessful.

A short convalescence with relatively rapid return to normal daily living was the rule. No deaths occurred.

We believe that this infection represents a separate disease entity, but judging from other reports, do not believe that it is a new disease. It does not appear to be related to the common cold, nor to epidemic influenza. Epidemiological observations indicate that it is contagious and suggest an incubation period of seven to eleven days. What bacteriological studies have been done fail to incriminate any of the known bacteria as etiologic factors. This negative evidence, plus certain characteristics of the clinical picture, at least suggest that this is a virus disease. So far, however, no positive evidence in favor of this impression has been obtained.

2 Shady Hill Square.

*During the four years under consideration there have been 235 cases of pneumonia of all kinds occurring among Harvard students. This includes patients taken care of by their own physicians at home or in hospitals and those at Stillman Infirmary. Three deaths occurred, all in the year 1935–1936, one a Type 1 lobar pneumonia, another a Type 3 lobar pneumonia and the third an overwhelming streptococcal pneumonia.

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SULFANILAMIDE THERAPY IN CHRONIC UNDERMINING STREPTOCOCCAL ULCER*

Report of a Case

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BOSTON

CHRONIC, undermining, streptococcal ulcers, though uncommon in general practice, offer a real problem in therapeutics. Numerous bacteriostatic and bacteriocidal drugs, vaccines, maggots, radiation therapy, and even surgical and electrosurgical excision, have frequently enough proved ineffectual in preventing the spread of these ulcers.

The comprehensive studies of Meleney and his co-workers[1-4] have added much to the knowledge of this condition. In his experience a microaerophilic, hemolytic streptococcus has been the principal bacterial agent. He found that zinc peroxide, which liberates nascent oxygen in close proximity to these organisms buried in the infected ulcer tissue, was very effective in healing many of the ulcers. At least two other authors[5, 6] report success with this preparation. It is evident, however, that not all these ulcers are cured by zinc peroxide.[7] The acknowledged variability in the oxygen-liberating potency and therapeutic efficiency of commercially available zinc peroxide may be one reason for this failure. Furthermore, the technical requirements necessary for the successful application of this drug as outlined by Meleney may prove difficult in the home and in some small hospitals.

Experience with the case to be reported and that of Goodman[8] indicates that sulfanilamide is very effective in the healing of certain of these chronic undermining ulcers. The ease of administration of this drug further simplifies the treatment. The only necessary laboratory studies are periodic blood counts. Blood sulfanilamide determinations may be performed if desired. Wound cultures are important in evaluation of results.

In this paper a successful outcome in the case of one of these ulcers from the administration of sulfanilamide is described. Approximately 8400 gr. of sulfanilamide was given over a period of three months without more than a slight transient effect on the bone marrow and on liver and kidney function.

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CASE REPORT

M. D., a 15-year-old school girl, was admitted to the Surgical Service at the Massachusetts Memorial Hospitals on August 17, 1938. Two and a half months previously, she had sustained a floor burn in the school gymnasium, the affected area being just below the knee on the anterolateral aspect of the left leg. Iodine was applied by the patient, but a moderate degree of infection developed. She was then treated in a clinic, and ammoniated mercury ointment dressings were used during a 2-week period. There was progression of the lesion despite this treatment, an ulcer with undermined edges and a central sinus being formed. Surrounding acute cellulitis required wet dressings for a few days. Incision and drainage of the central sinus was done on June 18. Within a week, an exacerbation of the acute cellulitis occurred requiring hospitalization for several days. During the following 6-week period — prior to admission at the Massachusetts Memorial Hospitals — the ulcer remained in an indolent state, not improving with ointments and other local treatments. The patient walked with difficulty owing to pain on moving the knee. There was little spontaneous pain in the ulcer. Her general health was not impaired. The past history was negative except for an intermittently running ear of several years' duration.

Physical examination revealed a well-developed and well-nourished girl. The color was good. There was a moderate degree of acne vulgaris. Systemic examination was generally negative aside from the left lower extremity. On the anterolateral aspect of the left leg was a roughly ovoid ulcer, 9.0 by 7.0 by 0.8 cm., its upper margin being just below the head of the fibula. It extended part way onto the calf laterally, where the bed of the ulcer was apparently formed by the aponeurosis of the soleus muscle. Soft granulations with a moderate degree of infection lined the open bed. The lateral margin was deeply undermined and draining thin, yellow-gray pus, with a slightly musty odor. There was shallow undermining in two places along the superior and medial margins of the ulcer. The surrounding skin for a distance of 3 to 6 cm. showed a scaling, eczematoid lesion. Motion was free in the joints of this extremity. Muscle function seemed

normal, although there was slight atrophy of disuse. No regional lymphadenopathy was found.

Urinalysis was entirely negative. The blood nonprotein nitrogen was 27 mg. per 100 cc., and the blood sugar 111 mg. The Wassermann and Kahn tests were negative. The white-cell count was 10,700, with 75 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes and 2 per cent endothelials. The hemoglobin was 78 per cent, and the red-cell count 4,450,000. X-ray films of the knee region revealed only bone atrophy.

The day after admission, under nitrous oxide and ether anesthesia, the sinuses at the ulcer margins were laid open and the infected granulations were curetted out. Cultures from this material showed an aerobic hemolytic streptococcus, *Staphylococcus aureus* and *Staph. albus*. No anaerobic or microaerophilic organisms were identified. Examination of smears failed to demonstrate fungi, yeasts or tubercle bacilli. The pathologist's report on sections of this material was "acute and chronic inflammation; granulation tissue."

Under the influence of wet saline and Dakin's solution dressings, during the next 2-week period the ulcer bed became cleaner, but did not decrease in size. The surrounding skin was somewhat macerated. The culture results continued to be the same, although but few organisms were found in the smears.

On September 12, 1 month after admission, dressings of active zinc peroxide paste were instituted according to the technic of Meleney.[2] The granulations became clean and solid, and healthy epithelium began to grow in from the margins. Progress was so favorable that the area was pinch-grafted on September 19, the zinc peroxide being continued with only a 24-hour interruption. After an 8-day period the grafts became liquefied. There was an exacerbation of the infection in the ulcer bed. The granulations were gelatinous and purple-gray, and exuded an excess of thin, gray pus with a musty odor. Cultures taken at this time yielded *Bacillus pyocyaneus*, in addition to a hemolytic streptococcus and *Staph. aureus*. Technical difficulties were then encountered in the use of the zinc peroxide. The material obtainable was very low in nascent-oxygen production (by Meleney's test-tube determination). Either because of this factor or because of the presence of the new organism, the zinc peroxide proved ineffective. Dressings moistened with 2 per cent acetic acid were used for several days, with definite improvement, and by the end of September the ulcer had decreased to roughly 4 cm. in diameter. The bed was shallow. In the next 2 weeks, however, a relapse occurred, the area becoming larger despite resumption of both acetic acid and zinc peroxide dressings for adequate treatment periods. *B. pyocyaneus* continued to be present in cultures for the next 6 weeks.

X-ray therapy (344 r in seven treatments — 200 kv., unfiltered) was given over a period of 10 days. For control purposes saline dressings only were used locally. The response to the x-ray treatment was unfavorable, the ulcer becoming larger during this period (Fig. 1). On October 19, the patient was started on sulfanilamide therapy, given with appropriate amounts of sodium bicarbonate by mouth. This was continued with the dosage ranging from 80 to 100 gr. daily in divided doses until the middle of January, 1939. During that time the ulcer healed in gradually, the response to the sulfanilamide being very convincing, and certainly more consistent than that to any of the other treatments used. It was necessary to discontinue the drug for a number of days on several occasions because of the destructive effect on the red blood cells, which fell as low as 2,600,000 per cubic millimeter. Four transfusions were given, the first on December 19, with a satisfactory resultant rise in the red-cell count. The white cells were not affected, and the patient had no constitutional reaction of significance. Mild cyanosis was observed at times, and moderate anorexia occurred when

FIGURE 1. *The Ulcer at the Start of Sulfanilamide Treatment — October 21, 1938.*

large doses were being given. On several occasions during the enforced rest period from sulfanilamide minor exacerbations of the ulcer activity occurred; the change from the infected, malignant-appearing, spreading, purple-gray granulations present at such a time to a relatively clean ulcer, within 48 hours after resumption of the sulfanilamide, was quite dramatic. The sulfanilamide level, taken frequently during this period, ranged from 0.5 to

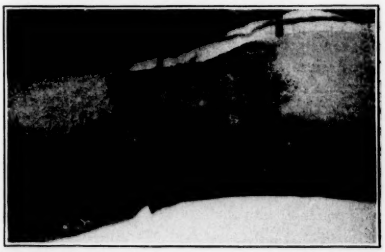

FIGURE 2. *The Ulcer in an Advanced Stage of Healing after Three Months of Sulfanilamide Treatment — January 16, 1939.*

3.4 mg. per 100 cc., being generally proportional to the dosage and the healing effect.

The majority of the pinch grafts planted November 26, during the course of sulfanilamide treatment, took, and acted as foci from which epithelium spread over the ulcer.

Small doses of sulfanilamide (40 gr. daily) were effective during January and February, but when the drug was entirely omitted exacerbation of the ulcer took place (Fig. 2). By February 25 only two tiny granulating

points remained, and it seemed feasible to discontinue the sulfanilamide. A total of 8400 gr. had been given. Cultures showed only *Staph. aureus.* The eczematoid reaction of the surrounding skin persisted for some time thereafter, but the ulcer was entirely healed by the time of discharge, in March, 1939. The function of the leg was normal. The patient's general health was excellent. The peripheral blood picture was normal.

The patient returned to the hospital 3 months later for a general check-up. At that time the skin over the previous ulcer area was solid, although still somewhat thin. There was moderate fibrosis of the subcutaneous tissues. The leg function was normal. Tests of kidney and liver function were within normal limits.

Comment

The ulcer described above stubbornly resisted various forms of treatment for two months. Dakin's solution, simple saline dressings and dilute acetic acid all seemed effective in cleaning up the lesion at times, even promoting a degree of healing. Exacerbation of the ulcer activity then invariably occurred. Zinc peroxide at first appeared even more effective. When, however, an attempt was made to pinch-graft the clean ulcer base, the grafts promptly sloughed and the ulcer again became active. Zinc peroxide paste was ineffective when tried on three subsequent occasions. This failure may well have been due to the inferior oxygen-liberating power of the material available. The complicating organism, *B. pyocyaneus,* present in the ulcer at this time may also have had some influence. X-ray therapy was entirely ineffective.

After the initial treatment period of two months, the ulcer was only a little smaller than on admission. There was less undermining, but the granulations of the base were still heavily infected. Sulfanilamide treatment begun at that time gained control of the inflammatory process within four days. Epithelialization, however, was slow. Through their experiments with dogs, Bricker and Graham[9] have shown that sulfanilamide exerts some inhibitory effect on wound healing. This may well be true in clinical practice also. The periods of rest from the sulfanilamide, necessitated by significant drops in the red-cell count, also added to the total healing time. Resumption of the drug on each occasion demonstrated convincingly its prompt effect on the inflammatory process.

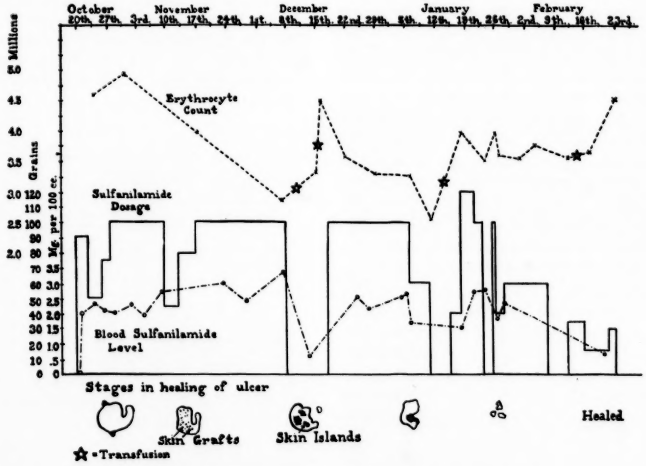

Figure 3. *Sulfanilamide Dosage in Relation to Erythrocyte Levels.*

It is rarely necessary to administer sulfanilamide in such high total dosage (8400 gr.) for so prolonged a period (four months). When one recalls the great interest shown in toxic side effects of this drug during recent months,[10] this case is of some importance in indicating the quantities which can be administered safely to a nonsusceptible individual. Moderate reduction in the red-cell count and a slightly diminished renal function during the treatment period were the only significant toxic effects. Three months later a check-up of the peripheral blood picture and the renal and hepatic functions by standard methods showed normal findings.

Despite daily dosages of 100 gr. of sulfanilamide

for long periods, it was never possible to raise the blood serum level above 3.4 mg. per 100 cc. The low serum sulfanilamide level may have accounted in part for the absence of serious side effects.

Approximately 60 gr. of sulfanilamide daily was required to maintain the ulcer in a healing phase, with a dosage of 80 to 100 gr. (2 or 3 mg. per 100 cc. serum level) as a safe margin. This affords an interesting comparison with Goodman's[8] findings. In his 2 ulcer cases, which were similar to that described herein, daily sulfanilamide dosage of 40 to 60 gr. was adequate to promote healing. Daily dosage of 120 gr. for a short period in our case resulted in no additional improvement in the healing and gave the patient anorexia and mild cyanosis. There was no febrile reaction on resumption of the sulfanilamide in full doses after a rest period, or at any other time. The patient experienced no reaction after any of the four transfusions, nor was there any ill effect from simultaneous administration of ferrous sulfate and the sulfanilamide, over fairly long periods.

Figure 3 illustrates the course of the sulfanilamide administration, together with the levels of the blood sulfanilamide obtained and the effect on the erythrocyte count. The leukocyte count ranged between 6000 and 16,000. Since it did not seem significantly influenced by the sulfanilamide, it is not shown in the graph.

No microaerophilic hemolytic streptococci were recovered from this ulcer. The strain was beta hemolytic and seemed to grow well in air. In one culture a poor growth of *Str. viridans* was identified, after periods of both zinc peroxide and sulfanilamide treatment. Clinically, however, the ulcer resembled the type described so adequately by Meleney and from which he was able to isolate microaerophilic organisms. The admittedly good control of the ulcer activity obtained by the first and potent lot of zinc peroxide seems to justify further the classification of this ulcer with Meleney's group.

A combination of zinc peroxide dressings—when a more constantly potent product can be developed—and sulfanilamide, administered systemically, may well prove the ideal treatment for this serious disease.

Summary

The healing of a resistant, chronic, undermining streptococcal ulcer following the administration of sulfanilamide is reported.

The salient features of this case were the prompt and convincing subsidence of the inflammatory process and institution of healing in the ulcer from the use of sulfanilamide, in contrast with other methods of treatment; and the absence of any but transitory and mild toxic effects from the administration of 8400 gr. of sulfanilamide during a period of four months.

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CLINICAL SIGNIFICANCE OF ORAL LESIONS IN ACUTE LEUKEMIA

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THE recognition of the importance of mouth lesions in various systemic disorders is of comparative recent date. Among others, Marshall and Lucia[1] have emphasized that many diseases of the blood present their most important signs and symptoms in the mouth. Love[2] found that 82 out of 152 cases of various types of leukemia showed oral lesions, and Musser[3] states that in acute leukemia oral lesions are usually present. A study of blood dyscrasias in the past four years has amply borne out these statements.

Leukemic manifestations in the mouth are mainly confined to the gingival tissues and mucous membranes. The commonest lesion is bleeding from the gums, the mechanism of which is not fully understood. Probably it is due in part to infiltration of the bone marrow by leukemic cells, which crowd out or inhibit the megakaryocytes with a resulting platelet deficiency. Subsequently secondary infection and ulceration may occur, or injudicious surgical procedure may result in necrosis and gangrenous stomatitis.

TABLE 1. *Oral Lesions in Cases of Leukemia.*

CASE No.	SEX	AGE	DIAGNOSIS	ORAL LESIONS
		yr.		
1	M	23	Subacute myelogenous leukemia	Gingivitis; bleeding from gums
2	M	30	Acute myelogenous leukemia	Ulcerative stomatitis
3	F	58	Acute monocytic leukemia	Ulcerative stomatitis
4	F	50	Acute monocytic leukemia	Ulcerative stomatitis
5	M	39	Acute myelogenous leukemia	Gingivitis; pain in jaw
6	F	38	Acute lymphatic leukemia	Pain in the jaw and bleeding from gums
7	M	52	Acute myelogenous leukemia	Bleeding from gums
8	M	17	Acute myelogenous leukemia	Bleeding from gums
9	F	13	Subacute myelogenous leukemia	Bleeding from gums
10	F	5	Acute lymphatic leukemia	No oral lesion
11	M	15	Acute myelogenous leukemia	No oral lesion
12	F	62	Acute monocytic leukemia	No oral lesion

Infiltration of the gums by leukemic cells occurs in acute leukemia. This results in swollen gums, which are painful and bleed easily on slight trauma. At times this swelling is so extreme that the gums cover the teeth. Ulceration and necrosis occur very frequently.

In the series presented here (Table 1), the patients with leukemia had bleeding, pain or infection of the gums, with or without ulcerative stomatitis.

Clinically, oral lesions in acute leukemia are important not only because they occur in a large percentage of cases, but also because very frequently they are the earliest sign of the disease. Of the 9 patients of this group with oral signs, 7 first visited the doctor or dentist because of bleeding from the gums, "trench mouth" or pain in the jaw. The following cases illustrate this.

CASE 1. J. C., a 23-year-old man, complained of a sore mouth, pain in the teeth and swollen, bleeding gums. He was treated by a dentist for "trench mouth" and his mouth improved. However, 3 months later his gums again bothered him and in addition he developed anorexia, became tired easily and felt run down. Because of weakness and loss of weight he was admitted to the Carney Hospital 7 months after the onset of his sore mouth.

Physical examination revealed an acutely ill man. His gums were swollen and pale, but there was no ulceration or evidence of petechial hemorrhage. There was a murmur at the cardiac apex, but no other findings in the heart and lungs. The liver and spleen could not be felt, nor were there any palpable lymph glands. The red-cell count was 1,650,000, the white-cell count 17,200, and the hemoglobin 35 per cent (Sahli). A stained smear revealed markedly diminished platelets, anisocytosis and poikilocytosis. A differential count showed 12 per cent lymphocytes, 10 per cent adult polymorphonuclears, 39 per cent band forms, 30 per cent myelocytes and 9 per cent myeloblasts. A diagnosis of myelogenous leukemia was made. The patient went steadily downhill and died 2 months after admission.

CASE 2. C. McP., a 30-year-old man, visited his physician for treatment of a badly infected mouth. The gums were bluish-black, and there was a foul exudate over the mucous membranes. The mouth under conservative treatment improved considerably. However, the patient's general condition became worse and he developed generalized edema, marked pallor, weakness and fever. One month after the mouth lesion developed he was confined to bed. Blood studies made at this time showed a hemoglobin of 15 per cent (Sahli), a red-cell count of 1,550,000 and a white-cell count of 58,600. A differential count showed the cells to consist almost entirely of myelocytes and myeloblasts; very few platelets were present. The red cells showed marked variations in size and shape, and many were nucleated. At this time the gums were very pale but were otherwise free of infection or bleeding. Throughout the illness there were no enlarged lymph nodes and neither the spleen nor the liver was palpable. One week after the blood study revealed the underlying disease, the patient died.

As pointed out by Forkner[4] and others, gangrenous stomatitis is especially prone to occur in acute monocytic leukemia. Forkner states: "In acute monocytic leukemia, diffuse swelling of the gingivae with a tendency for the teeth to become submerged in the gums is encountered in the

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great majority of cases." He believes that the oral lesions in acute lymphatic and acute myelogenous leukemia are usually nonspecific. Osgood[5] reviewed cases of monocytic leukemia, and reported that gingival swelling was noted in 80 per cent of 88 cases in which the gums were mentioned. Not all investigators agree with Forkner that the infiltrative lesion is almost always pathognomonic of acute monocytic leukemia, but in general it is well recognized that gingival involvement is frequent in acute leukemia.

In the present series there were 3 cases of acute monocytic leukemia, and in 2 of them (Cases 3 and 4) extensive necrotic and ulcerative lesions developed from what at first appeared to be "trench mouth." The mere presence of Vincent's organisms and other secondary bacterial invaders should not lead to this diagnosis, as it implies a purely local process. In both cases mentioned, patients first visited the dentist, but the progressive character of the gingival lesions, with the rapid onset of pallor, fever and prostration, led to further investigation and the discovery of the background of acute leukemia.

Not infrequently cases have been reported illustrating the disastrous results of tooth extraction or other oral surgery. Recently Klumpp and Evans[6] in a paper recording 8 cases of monocytic leukemia stated that 5 of these were discovered following extraction of teeth. In this regard the following 3 cases are of interest.

Case 5. R. P., a 39-year-old man, visited a dentist because of pyorrhea, bleeding gums and pain in the lower jaw. His lower incisors and bicuspids were removed, and 1 week later he was admitted to the Carney Hospital with extensive gangrene of the mouth. The hemoglobin was 48 per cent (Sahli), the red-cell count 2,600,000 and the white-cell count 69,000. The stained smear showed cells which appeared to be stem cells of the myeloid group. The patient died 48 hours after admission. Autopsy confirmed the diagnosis of acute myelogenous leukemia.

Case 6. C. D., a 38-year-old woman, went to the dentist because of pain in the jaw. No local lesions which would account for this pain were found, but the patient insisted that the teeth be removed. Subsequent to the extraction she bled profusely from the sockets and then developed generalized oozing from the gums. Because of weakness, fever and severe epistaxis she entered St. Elizabeth's Hospital several weeks later. The laboratory findings were as follows: hemoglobin 20 per cent (Sahli), red-cell count 1,400,000 and white-cell count 1200. The stained smear showed markedly reduced platelets with white cells which were entirely of the lymphocyte group. Most of these were adult lymphocytes, but several lymphoblasts were found, and a diagnosis of acute lymphatic leukemia was made. Bone-marrow biopsy substantiated this diagnosis, and soon afterward the patient died.

Case 7. S. K., a 52-year-old man, had a molar extracted from his upper jaw and developed pain and bleeding at the site of extraction. The gum failed to heal, and he developed weakness, general malaise and aching pains in the gums. When admitted to the Somerville Hospital 1 month later he had diffuse ulceration and pyorrhea of the gums, with necrotic material in the unhealed socket. Otherwise the physical examination was essentially negative. The laboratory findings were as follows: hemoglobin 38 per cent (Sahli), red-cell count 1,820,000 and white-cell count 2750. The stained smear showed 2 per cent adult polymorphonuclear leukocytes; the remainder of the cells looked like large lymphocytes, but an oxidase stain identified them as promyelocytes, and bone-marrow biopsy substantiated the clinical diagnosis of myelogenous leukemia. This patient left the hospital. He died about six months later.

In the remaining 5 cases there was bleeding from the gums in 2 (Cases 8 and 9), and no oral lesions in the other 3. In Case 8 retinal hemorrhage with blindness was the initial and outstanding manifestation, although severe bleeding from the gums also occurred early in the course of the disease. Jaundice, enlarged liver and spleen and an aleukemic blood picture featured the course of Case 9. The patient developed bleeding from the gums, but this disappeared with the jaundice. For several months she was practically free of symptoms, but she finally succumbed after developing a blood picture typical of myelogenous leukemia.

Discussion

Physicians and dentists should be encouraged not to regard the oral cavity as an entity, but rather to consider that the mouth has often the same relation to the body as have the eyegrounds, and frequently will be found to reflect underlying systemic disorders. Whenever they are confronted with apparently benign bleeding or gingivitis they should not fail to inquire into all the possibilities. Locally, pallor, ulceration and petechial hemorrhages of the mucous membranes, tonsillar enlargement and the presence or absence of glandular swelling in the neck should be noted. The prognosis should be guarded when there is severe stomatitis, especially in a patient with fever, pallor and dependent edema.

Acute leukemia is not a common disorder, and there are many diseases that may have oral manifestations of a similar type. In many cases a diagnosis by local investigation alone is impossible. Severe sepsis, agranulocytosis, infectious mononucleosis, essential purpura, hemophilia, scurvy, aplastic or myelophthisic anemias and rarely pernicious anemia may give rise to serious diagnostic difficulties, especially in the differentiation from aleukemic and leukopenic leukemias. Both the clinical course and routine blood studies in these atypical leukemias may be misleading; in any event the patient must be given the benefit of the doubt, and specific therapy, when possible, administered as early as compatible with good clinical judgment. On the other hand, indiscriminate

therapy before a diagnosis has been established should be deplored. Every reasonable clinical and laboratory test necessary for diagnosis should be applied before blood transfusion, Pentnucleotide, liver extract and chemotherapy have so confused the situation that a true picture of the case is impossible.

Conclusions

Oral lesions are frequent in acute leukemia, and are prone to occur early in the course of the disease.

Accurate diagnosis is important, in order that those conditions which simulate certain types of leukemia may be differentiated and early therapy be instituted.

It is evident that acute leukemia is an invariably fatal disease, but palliative measures and the avoidance of injudicious oral surgery will make the sufferer much more comfortable.

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ONE-STAGE LOBECTOMY IN BRONCHIECTASIS*

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THE historical aspect of the development of pneumonectomy and lobectomy in man has been presented by numerous authors, notably Ballon, Singer and Graham,[1] Haight[2] and Heuer.[3] Dissatisfaction with the one-stage lobectomy for bronchiectasis early in the century was materially lessened by the development of the multiple-stage attack, together with the perfection of anesthesia, the employment of new diagnostic methods and the better understanding of thoracic physiology. All these improvements rendered more feasible the approach to the ideal operation, namely a reasonably safe one-stage procedure. A turning point in this direction came with the work of Brunn,[4] published in 1929, at which time he reported 6 one-stage lobectomies with 1 death. In 1933 Alexander[5] presented a two-stage procedure with a mortality below 20 per cent. The first stage consisted of creating adhesions between the healthy lobes and the chest wall so as to reduce the size of the pleural cavity and stabilize the mediastinum. In a review published in 1934, Heuer[3] stated that the two-stage procedure still had the lowest individual mortality, although he predicted that the one-stage operation would become more frequent. Churchill[6] in 1936 reported a mortality of 6 per cent in 49 cases covering the years 1929 to 1935. In 18 cases the one-stage procedure was employed. At present it is probably true that most surgeons prefer the one-stage method, but reserve the multiple-stage attack for certain cases.

This article reports 5 cases of unilobar bronchiectasis in which lobectomy was performed in one stage. These cases represent all the one-stage lobectomies performed at the Hitchcock Clinic for simple unilobar bronchiectasis, and in this group there has been no mortality. Lobectomy in cases with bilateral disease, tumor and tuberculosis is not considered at this time.

All cases were fully investigated for the presence of tuberculosis. Particular attention was paid to even moderate degrees of secondary anemia, which was present in 3 cases. All patients were bronchoscoped prior to operation. Postural drainage was instituted routinely, and close supervision was given in order to ensure favorable results. Adequate time was allowed to get the patient in the best possible condition for operation.

Intravenous saline and glucose were started just before operation by tying a cannula in an ankle vein. Avertin was administered on the 80-mg. scale, and nitrous oxide and ether were introduced through the Flagg type of intratracheal tube. In the lower lobe cases the seventh rib was resected in the posterolateral aspect. In the upper lobe case the incision was made through the bed of the sixth rib. The Bethune modification of the Shenstone tourniquet was employed at the hilus. Closure of the hilar stump was obtained by mattress sutures of catgut.

Drainage was employed in 4 cases. In Case 2 (upper lobe) no drainage was employed, and empyema resulted. In 3 cases drainage was done by means of a No. 24 urethral catheter inserted posteriorly just above the diaphragm, moderate

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suction being applied at the bedside. In Cases 4 and 5, in addition to the posterior catheter, a Pezzer catheter was inserted anteriorly, and 6 to 8 cm. of water suction was applied to both tubes. Re-expansion of the lung was greatly facilitated by this procedure. In these 2 cases bronchoscopic aspiration of the tracheobronchial tree was carried out immediately at the close of the operation. It resulted in marked improvement in the oxygenization and comfort of the patient in the first postoperative hours. All 5 patients were given a transfusion of citrated blood during or immediately after operation. The oxygen tent was employed routinely, but only for a few hours in Cases 4 and 5.

In Case 1, mild hemoptysis occurred a year after lobectomy. This was successfully treated by bronchoscopic cauterization of the left lower lobe stump. There has been no recurrence in two years. In Case 2, a hemolytic streptococcus empyema occurred, which was successfully treated with Prontosil. However, the cavity left by lobectomy failed to close, and the empyema recurred a year after operation. This was treated by thoracostomy, followed by a regional thoracoplasty for closure of the cavity. There has been no further trouble in a year and a half. In Case 3, a mild wound infection developed but cleared promptly with drainage. In Cases 4 and 5 there were no complications.

All the patients were free of cough and sputum and were able to carry on their normal occupations. In Case 1 a postoperative Lipiodol injection showed a slight saccular end of the bronchial stump at the point of amputation. The patient was entirely well, however, and has been through two winters without trouble.

Case Reports

Case 1. C. M., a 32-year-old, married woman, was admitted July 15, 1936. Except for an attack of pneumonia in childhood, she had been in perfect health until 3 years before admission, when she had a small hemoptysis. At that time the hemorrhage was considered to have come from the nose or throat, and although the lungs were examined with a stethoscope no x-ray film was taken, and the patient was considered well. One year before admission, while sitting quietly in a chair, she had a second hemoptysis of a mouthful of blood. An x-ray film was negative, and a tuberculin test also was negative. Repeated sputum examinations failed to show tubercle bacilli. Five weeks before admission she had a severe pulmonary hemorrhage, the blood spurting from her mouth, and she lost nearly a quart of blood. Again sputum examination and a tuberculin test failed to indicate any disease process.

Physical examination on admission showed a rather pale, sallow, undernourished woman in a nervous condition. The entire examination was negative. The red-cell count was 3,700,000, and the white-cell count 5800. Urinalysis was negative, and sputum tests for tuberculosis also were negative. Plain x-ray films of the chest were negative, except for an old healed tuberculous infection of the right hilus nodes. Bronchoscopic examination was negative. Lipiodol injection showed bronchiectasis of the medial bronchi of the left lower lobe, with some atelectasis and failure of alveolar filling (Fig. 1).

On July 30, under intratracheal anesthesia, a posterolateral incision was made, and it was found that the lower lobe was densely adherent to the diaphragm by vascular adhesions. There was an incomplete separation between the upper and lower lobes, so that the tourniquet was applied to the lower lobe and the base of the upper. The stump of the lower lobe was secured with mattress sutures. There were no adhesions between the upper lobe and the chest wall. A No. 24 urethral catheter was

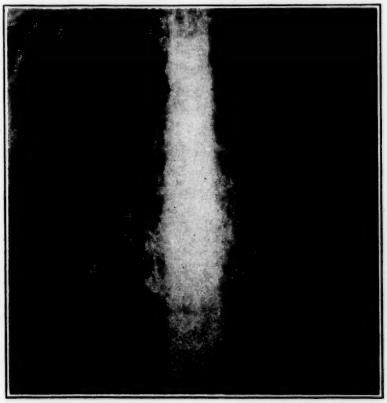

Figure 1. *Case 1.*
Atrophic bronchiectasis of the left lower lobe, with atelectasis.

inserted through a trocar wound in the posterolateral aspect of the chest just above the diaphragm, and the wound was closed in layers. Moderate suction was placed on the catheter as soon as the patient had been returned to the ward. The pathological diagnosis was atrophic bronchiectasis and chronic pneumonitis.

In the first 48 hours after operation some difficulty in raising sputum was encountered, but this was lessened by postural drainage; the patient coughed up some blood-streaked mucus. The drainage tube was removed on the 8th postoperative day. The temperature rose as high as 101°F. on each of the first 5 postoperative days. It then gradually declined to normal. The patient was discharged on the 27th postoperative day. An x-ray film taken at discharge showed that the left lung was completely expanded. The lung fields were clear except for the remains of Lipiodol at the right base. The heart was displaced slightly to the left.

On December 28, 1937, the patient had another small hemoptysis. She was readmitted to the hospital, and bronchoscopic examination showed an area of granulation tissue in the bronchial stump of the left lower lobe. This was cauterized, and for the last 2 years the patient has

been perfectly well and has gained weight. She has had no cough or sputum, and no complaints.

Case 2. R. L., an 18-year-old girl, was admitted on January 25, 1937, complaining of persistent cough productive of foul-smelling sputum, amounting sometimes to 100 or 150 cc. a day. She had had several attacks of pneumonia in childhood, each one leaving her with more cough. Five years before admission the sputum increased in amount and became foul-smelling. There was an occasional frank hemoptysis. The patient could not take part

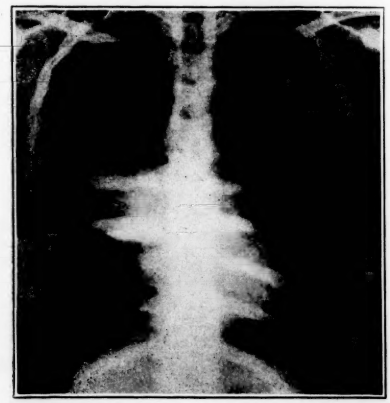

Figure 2. *Case 2.*

Appearance of the cyst on admission to the hospital. Note the fluid level and the small amount of Lipiodol in bottom of the cyst.

in social activities because of the frequency of the cough and the foulness of the sputum. Routine x-ray films taken at school 1 month before admission showed a lesion in the right upper chest. The patient was sent to another hospital, where a Lipiodol injection was done. Following this examination she became very ill, with fever, sweating and weight loss. The sputum increased to 250 or 300 cc. a day, and she was unable to lie down for fear of choking.

Physical examination showed a sallow-complexioned girl, fairly well nourished and not acutely ill. There was a frequent cough productive of foul sputum. The patient was unable to lie flat in bed because of the cough. Examination of the chest revealed impaired resonance and decreased aeration of the right upper lobe. There was marked clubbing of the fingers. The temperature was 99.8°F. The red-cell count was 4,310,000 and the hemoglobin 13 gm. There were 12,500 white cells, with 57 per cent polymorphonuclears and 27 per cent lymphocytes. The urine showed 0.007 gm. of albumin; otherwise the examination was negative. Examination of the sputum showed no spirochetes, a few pneumococci and numerous streptococci. Repeated examinations failed to show tubercle bacilli. An x-ray film of the chest showed a large, round cavity 8 cm. in diameter in the mid-portion of the right lung (Fig. 2). The cavity was half-filled with fluid, with a small amount of Lipiodol at the bottom. The wall was extremely thin, and there was no reaction in the surrounding lung. The medial wall of the cavity was in contact with the mediastinum; in the lateral view the anterior wall was in contact with the anterior wall of the chest, the location being in the lower portion of the upper lobe. The lung fields were otherwise clear. The x-ray diagnosis was congenital lung cyst with bronchial communication. The patient improved remarkably on postural drainage. She received three injections of neoarsphenamine. On February 2, 8 days after admission, an x-ray film showed that the upper lobe cyst had been emptied of its contents. The temperature at this time was normal, and lobectomy was advised.

The right upper lobe was removed on February 16. A posterolateral incision was made, with resection of the sixth rib. The pleural space over the upper lobe was completely obliterated by rather dense adhesions, some of which were quite vascular. The lower and middle lobes were also adherent to the chest wall. A segment of the seventh rib was also resected to improve the exposure, and the lobe was dissected away from the chest wall and mediastinum. It was seen that the cyst in the anterior surface of the upper lobe was provided with a separate

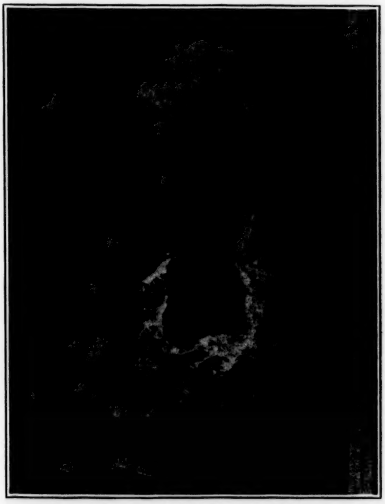

Figure 3. *Case 2.*

Surgical specimen, showing the cyst and the atelectatic upper lobe.

bronchus arising from the right upper lobe bronchus. Tourniquets were placed about the hilus of the latter, and the lobe was amputated. The stump was secured with mattress sutures, and the chest was closed without drainage (Fig. 3). The pathological diagnosis was bronchial cyst, congenital. It is possible that the cyst could have been dissected away without complete removal of the lobe, but it was thought to be too deeply imbedded.

The patient reacted very well after the operation. The

temperature rose to 101°F. the next day, and on the following day to 102. Thoracentesis on the 7th day yielded fluid which gave a pure culture of hemolytic streptococci. The infection was treated by injecting Prontosil into the cavity and also intramuscularly. On the 21st postoperative day the chest fluid was sterile, and from then on the course was one of rapid improvement, the temperature returning to normal. The patient was discharged on the 33rd postoperative day, at which time she had no cough or sputum. It was noteworthy, however, that the mid-

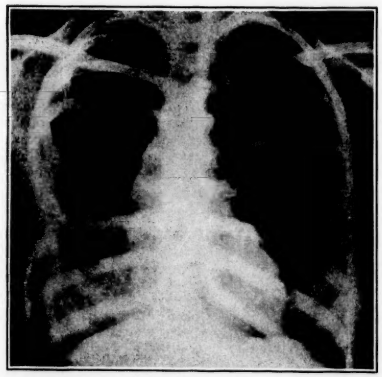

FIGURE 4. *Case 2.*

Cavity left after lobectomy due to failure of the lower and middle lobes to overexpand.

dle and lower lobes never overexpanded so as to occupy the space created by removal of the upper lobe (Fig. 4).

The patient remained well through the next year, without cough or sputum. She was readmitted, however, on January 22, 1938, with fever and pain in the right chest. The temperature rose to 104°F. each day, and the patient was obviously toxic. X-ray examination showed an accumulation of fluid in the space previously occupied by the upper lobe. The red-cell count was 4,000,000, and the white-cell count 11,700. Thoracentesis in this region resulted in the recovery of thick, green pus, which on culture showed non-hemolytic streptococci and pneumococci. Blood culture was sterile. It was considered that the bronchial stump must have opened and that the pleural cavity had become contaminated through this avenue. An incision at the anterior edge of the old lobectomy scar was made, and large quantities of pus were evacuated. The temperature immediately dropped to normal and remained there, and 21 days later a thoracoplasty was performed with resection of the first five ribs. The patient recovered rapidly from this procedure, obtained a good collapse of the cavity and returned home 16 days after the last operation. She has remained well during the year and a half following the last operation.

CASE 3. A. L., a 15-year-old girl, was admitted August 25, 1937. She gave a history of always having had "chest trouble." Since an attack of pneumonia at the age of 2 she had had a chronic cough with production of about 30 cc. of thick, yellow sputum a day. At the age of 5 she had a second attack of pneumonia, following which the sputum gradually increased. There were several other attacks of pneumonia, the last occurring in March, 1937. The patient was practically never without a "cold." Her general health was good. She was able to enjoy mild exercise and gained steadily in general development.

Physical examination showed a well-developed and nourished girl in no acute distress. The only positive findings were in the thorax, where the expansion of the left chest was greatly reduced and that of the right was exaggerated. Tactile fremitus and whispered voice were markedly increased over the left base posteriorly, and there were scattered moist rales over this area. There was structural scoliosis with convexity to the right. The red cells numbered 4,120,000 and the white cells 8300; the hemoglobin was 13.5 gm. X-ray examination showed the left side of the thorax to be considerably smaller than the right, with corresponding scoliosis of the thoracic spine. The entire lower half of the left lung field was obscured by homogeneous density. The upper portion of the lung appeared clear. The appearance was that of atelectasis of the left lower lobe. Lipiodol injection showed that there was a marked saccular bronchiectasis involving the entire left lower lobe, with marked atelectasis in this region.

FIGURE 5. *Case 3.*

Advanced saccular bronchiectasis of the left lower lobe, with atelectasis of the lobe and compensatory changes in the right lung. The scoliosis was probably due to atelectasis with pleural adhesions.

There was overexpansion of the right lung field, which extended a third of the way into the left thorax. This was considered to be a typical surgical case (Fig. 5).

Lobectomy of the left lower lobe was performed on November 10. The usual posterolateral incision was made. The left lower lobe was found to be dark red, firm and atelectatic. It was densely adherent to the chest wall, diaphragm and upper lobe. The base of the upper lobe was adherent to the chest wall. After lobectomy in the usual manner a No. 24 urethral catheter was inserted just above the diaphragm in the posterolateral aspect of the chest.

The pathological diagnosis was hypertrophic bronchiectasis, with marked chronic interstitial pneumonitis and fibrosis.

Immediately after the operation the patient ran a fever, which reached 102°F. on the 3rd day. This was found to be due to a wound infection, and when the latter was drained the temperature returned abruptly to normal. Convalescence was uneventful. The patient was discharged on the 39th postoperative day without cough or sputum.

The patient has been seen repeatedly in the follow-up clinic and has remained well. She goes through the winter with one cold and has no cough or sputum. There is considerable shift of the heart to the left, occupying the region of the lower lobe. The scoliosis is not improved.

CASE 4. E. T., a 31-year-old woman, was admitted July 10, 1938. She had had eight hospital admissions elsewhere, mostly for pelvic operations. In 1933 she was badly injured in an automobile accident, and was unconscious for several days. Her chief complaint at the time of admission was a productive cough since February, 1937, with frequent hemoptysis. There was frequent joint pain and weakness and fatigue during this time.

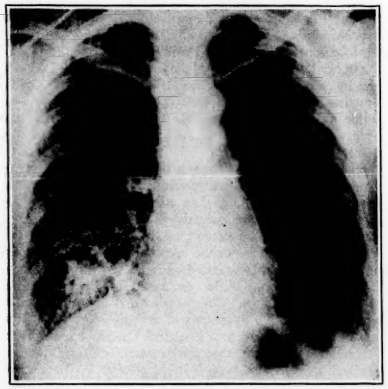

FIGURE 6. *Case 4.*
Moderate saccular bronchiectasis of the right lower lobe.

Physical examination was essentially negative, except for reduced aeration of the right lower lobe with occasional rales. The red-cell count was 4,900,000 and the white-cell count 6000. The hemoglobin was 16 gm. Repeated examination of the sputum was negative for tubercle bacilli. A tuberculin test was negative. At x-ray examination the lung markings at the right base were increased in width and density. In the lateral view these markings lay in the region of the lower lobe. Otherwise the lung fields were clear. Lipiodol injection showed saccular bronchiectasis of the lower lobe bronchi, associated with failure of alveolar filling (Fig. 6). The rest of the bronchi were normal. The patient returned home for some days and was readmitted on August 15.

At operation September 26 the lower lobe of the right lung was found densely adherent to the lateral chest wall. The base of the upper lobe was also connected to the chest wall by a few delicate strands. The fissure between the lobes was incomplete. The lower lobe was amputated in the usual manner. For drainage a No. 24 urethral catheter was inserted posteriorly and a No. 24 Pezzer catheter anteriorly. After closure of the chest, suction was placed on both catheters. At the end of the operation a bronchoscope was passed and the tracheobronchial tree was cleaned of secretions. The pathological diagnosis was chronic bronchiectasis.

The patient had an entirely uneventful postoperative course. The temperature reached 101°F. on the 3rd postoperative day, but rapidly declined to normal thereafter. X-ray examination of the chest the day after operation showed the right lung nearly completely expanded and practically no fluid present in the pleural cavity. The patient was sent home on the 21st postoperative day, having gained 4 pounds in the first 2 weeks following operation.

The patient has been free of cough and sputum, although she has had complaints referable to other parts of the body.

CASE 5. L. F., a 26-year-old man, was admitted May 1, 1939. He had had pneumonia at the ages of 15, 16 and 17. Five years previously he had developed a productive cough, which had been present ever since. He raised large quantities of foul sputum and was practically never without a "cold."

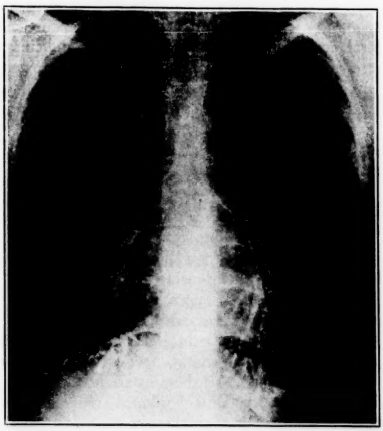

FIGURE 7. *Case 5.*
Moderate bronchiectasis of the right lower lobe.

Physical examination was essentially negative except for decreased aeration and scattered rales over the right lower lobe. The red-cell count was 4,650,000, and the white-cell count 17,050. Urinalysis was negative. Repeated examinations of sputum were negative for tubercle bacilli. Serological tests were negative. X-ray examination showed an increased density of the lower portion of the right hilus and of the lung markings running to the cardiophrenic angle. Otherwise the chest was negative. The appearance was that of an infection at the right base. Lipiodol injection showed a moderate saccular bronchiectasis of the

terminal bronchi of the right lower lobe posteriorly, with failure of alveolar filling and some evidence of atelectasis (Fig. 7).

At operation on May 3, no adhesions were encountered in the right thorax. After sectioning the inferior pulmonary ligament the lower lobe was amputated between tourniquets, and the stump was closed in the usual manner. A urethral catheter was inserted posteriorly and a Pezzer catheter anteriorly as in Case 4, and at the termination of the operation bronchoscopic aspiration of the tracheobronchial tree was carried out. The pathological diagnosis was bronchiectasis, with chronic suppurative pneumonitis and organized pneumonia.

The patient had a completely uneventful recovery. The temperature rose as high as 101°F. on the 2nd postoperative day, but rapidly declined to normal. He was allowed to get up on the 11th day and was discharged on the 18th day after operation.

The patient has remained free of cough and sputum, has gained weight, and is back at his work as a car salesman.

Conclusions

I believe that one-stage lobectomy is the procedure of choice in the treatment of bronchiectasis, and that with present-day methods it is reasonably safe. Multiple-stage operations should be applied to cases in which the patient is in poor general condition, or in which technical difficulties are expected in the presence of unusually extensive adhesions, so that the possibility of hemorrhage and manipulation may result in a prolonged and dangerous operative procedure.

Summary

Five cases of unilobar bronchiectasis are presented in which one-stage lobectomy was successfully performed. This represents the total experience at the Hitchcock Clinic with the one-stage operation for simple bronchiectasis of a single lobe. Preoperative measures, operative technic, complications and results are discussed.

It is pointed out that in 1 case there were very few adhesions between the normal lobe and the chest, and in 2 cases there were no adhesions. None of these 3 patients developed empyema, and in all, re-expansion of the lung was prompt.

The average postoperative hospitalization was twenty-seven days, the longest period being thirty-nine and the shortest eighteen.

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Discussion

Dr. Thomas H. Lanman, Boston: I agree with Dr. Tyson. He believes, as we do at the Children's Hospital, that it is very much safer to drain all these cases. All our 14 patients have had the one-stage operation that he advocates, and we have had the good fortune not to lose any. It is interesting that the histories of most of his patients suggest that the onset of the bronchiectasis dates back to childhood.

Dr. Harlan F. Newton, Boston: I agree with Dr. Lanman. In our series of lobectomies for chronic bronchiectasis at the Peter Bent Brigham Hospital, all these patients have been operated on by a one-stage procedure, which Dr. Tyson also used. Certainly it is now well established that in experienced hands it is possible to remove a lobe of a lung with a low operative mortality.

There are two points I should like to add which I know Dr. Tyson did not have time to elaborate on. In the first place, the great majority of my cases of chronic bronchiectasis involving the lower lobe of the lung treated by lobectomy have shown involvement of the lingula of the upper lobe, particularly if the interlobar fissure between the lobes is obliterated. Because of this it is my routine practice to remove the lingula of the upper lobe in a so-called lobectomy for lower lobe bronchiectasis; hence the operation should perhaps be called partial pneumonectomy rather than lobectomy.

The second point of interest is that, with the cause of bronchiectasis often obscure, removal of a definitely diseased lobe of the lung does not in every case ensure against recurrent bronchiectasis in the opposite lung. I have just seen such a patient, on whom I performed left lower lobe lobectomy at the age of seventeen, four years ago, and who at that time showed, by bronchoscopy, Lipiodol studies and other examinations, disease limited to the left lower lobe. She has also had no demonstrable sinusitis or chronic upper-respiratory infection. She now has definite tubular bronchiectasis of the right lower lobe.

I believe, therefore, that the problem is at present not so much the technical one of safely removing a portion of the lung for chronic infection, — for that has been demonstrated, — as it is a pathological one as to the origin of the primary disease and the prevention of its recurrence.

Dr. Tyson (closing): Regarding lingula involvement, we looked for this very carefully in our cases and were unable to demonstrate any disease in this area. Bronchiectasis that has been overlooked in the lingula and not treated will almost surely give rise to residual symptoms. If involvement of the lingula is present, this portion of the lung should be removed.

I wish to emphasize again that we found the use of two drainage catheters of the greatest help in the last two cases. I first saw Dr. Churchill use this method of facilitating re-expansion and drainage. Postoperative bronchoscopic aspiration, performed as soon as the intratracheal tube has been removed, is also of great assistance in promoting the comfort and oxygenization of the patient in the first twenty-four hours. This practice was suggested to me by Dr. Lindskog, of New Haven.

I do not believe that the reappearance of bronchiectasis after the removal of a diseased lobe is adequately proved, at least in any significant number of cases. I am inclined to think that if it is discovered subsequent to operation, the Lipiodol injection made before lobectomy may have been at fault.

REPORT ON MEDICAL PROGRESS

RECENT ADVANCES IN THE BIOCHEMISTRY AND THERAPEUSIS OF POTASSIUM SALTS*

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POTASSIUM salts have been employed in the treatment of disease for many centuries. It seems reasonable to believe that in most cases the indications for their use were based on practical experience and were not derived by rational deductions from experimental observations. Recent investigations have enlarged our knowledge of the action of potassium salts, and at present, indications for their use are more precise and less empirical. In this review no attempt will be made to discuss all the recent data concerning the role of potassium in the animal and human organism. Only certain evidence believed to be related to the argument will be presented.

THEORETICAL AND BIOCHEMICAL CONSIDERATIONS

The inorganic salts of potassium are highly ionized in the body. Little attention need be given, therefore, to the anion; the principal effects of the presence of potassium will be assumed to be produced by the cation. There is no recognized hormone in the body that regulates potassium exchange as desoxycorticosterone regulates sodium exchange or parathormone regulates calcium exchange. It is likely that at some future time a hormone or regulator for potassium will be discovered, the lack of recognition of which offers a formidable check on pertinent investigations.

There are three known isotopes of potassium, having atomic weights of 39, 40 and 41. More than 93 per cent of the potassium in animal tissue has an atomic weight of 39,[1] nearly all the remainder consisting of that with an atomic weight of 41. The isotope with the atomic weight of 40 is responsible for all or nearly all the radioactivity of potassium. It is extremely rare, and does not appear to be more concentrated in animal tissue than elsewhere in nature. No effects of naturally occurring potassium can be attributed with certainty to its radioactivity, nor have any biologic effects been observed experimentally from irradiated potassium salts that were unlike natural potassium.[2]

Of the several satisfactory methods for the determination of serum potassium, we believe that the one revised in our laboratory[3] possesses certain advantages. The range for serum potassium in healthy men is between 3.5 and 4.5 milliequiv. per liter (14 to 18 mg. per 100 cc.) in 90 per cent of the subjects; the extreme range is from 3.4 to 4.9 milliequiv. per liter.

In this presentation the role of potassium will be discussed under three divisions: as the principal base in tissues and blood cells it is concerned with the regulation of acid-base balance of the body; as an insulin-antagonistic and epinephrine-like substance, it participates in the intermediary metabolism of carbohydrates; as an antagonist of cholin esterase and as the principal base in muscle cells, it is concerned with the transmission of the nerve impulse to the muscle fiber and with the contractility of muscle. While we do not wish to engage in polemics concerning the chemical versus the electrical theory of conduction of the nerve impulse, it appears to us that the chemical theory best explains most experimental observations.

The recognition of the participation of potassium in neuromuscular physiology is recent. To be sure, Ringer,[4] Howell[5] and others showed that large amounts of potassium in perfusion fluid exert an effect on cardiac action, but only in the last decade have investigations produced data of interest to clinicians. Brown and Feldberg[6] showed that small concentrations of potassium chloride in perfusion fluid increase the response of sympathetic ganglia to "single submaximal preganglionic volleys." They observed also that potassium stimulates the cells of normal and denervated ganglia to discharge. Conversely, Vogt[7] showed that in the dog, prolonged faradic stimulation of the preganglionic fibers of the superior cervical ganglia produced a decrease in potassium content of the ganglionic tissue. At the motor end-plates potassium has an action antagonistic to that of curare,[8] and in this action it is similar to prostigmine,[9] guanidine, ephedrine and Congo red. This suggests that

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Paper No. 9 in Studies on Myasthenia Gravis, pursued by one of the authors (R. S. S.).

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potassium has an inhibiting effect on the action of cholin esterase. Lastly, Fenn[10] has shown that during muscular contraction potassium leaves the muscle and that not until recovery does it return. These and other significant investigations constitute advances in the clinician's understanding of disease.

In an attempt to simplify this presentation, it has been assumed that the several actions of potassium are independent, although it is likely that subsequent observations will not bear this out. For example, in Addison's disease the action of potassium may not be confined to any one of the three pharmacologic effects, and in the treatment of hay fever the epinephrine-like action may be associated with a change in acid-base balance or in neuromuscular function. It is quite possible that we are misinterpreting some of the actions of potassium, but for the sake of clarity they will be discussed separately and in the order given above.

Therapeutic Considerations

Potassium salts may be prescribed in various forms for oral administration. It is our experience that an aqueous solution of potassium chloride produces less gastrointestinal distress than does the administration of the salt in gelatin capsules or in tablet form. Usually a 25 per cent solution of potassium chloride is prescribed, one teaspoonful of which contains approximately 1 gm. of the salt. The quantity to be ingested is therefore easy to calculate. One teaspoonful may be added to a wineglassful of water, milk, fruit or tomato juice and ingested with little or no gastric distress. Occasionally patients complain that they have been unable to tolerate initial daily doses totaling 6 or 8 gm. of potassium chloride. Under such circumstances smaller doses are given at first and the amount is increased daily up to the maximum desired. Those who have been instructed in this manner have been able to take the quantity prescribed without untoward effects. A more detailed description of potassium administration in patients with myasthenia gravis is given below.

Edema

An accumulation of sodium chloride and water in the interstitial spaces is the invariable state in edema, whether this arises from renal, cardiac or hepatic failure. If a hypertonic solution of potassium chloride is given, a two-fold action results. Potassium competes with sodium for body water, and if an adequate amount is not available for both, a portion of the retained sodium is displaced and subsequently excreted in the urine. Secondly, potassium competes with sodium for reabsorption by the cells of the renal tubules, so that if a large excess of potassium is present in the glomerular filtrate, it depresses the sodium reabsorption and an additional loss into the bladder urine ensues.

In the treatment of edema, Barker[11] found that 5 gm. of potassium chloride was an effective diuretic. Keith and Binger[12] confirmed this observation in patients and observed, in addition, a diuretic action in normal persons. Mackay and Butler,[13] however, were unable to detect any significant increase in excretion of sodium or edema fluid following the ingestion of equal amounts of potassium chloride. There is no satisfactory explanation for this failure of agreement among the various experimental observations.

Addison's Disease

The data on patients with Addison's disease appear to be more definitive. This malady is caused in part by a failure in elaboration of one or more hormones of the adrenal cortex, and involves dissipation of sodium and water and retention of potassium and urea. Some authorities hold that the increased concentration of potassium is as important in the pathogenesis of certain symptoms as is the decrease in concentration of sodium. It follows that a high potassium intake may aggravate symptoms of adrenal insufficiency; conversely, a low potassium intake may be beneficial in the treatment of this condition. A practical test, based on this observation, has been devised by Wilder and associates[14] for suspected adrenal insufficiency. Five gm. of potassium citrate is given daily for approximately three days. The patient, meanwhile, is given a diet low in sodium content. A decrease in concentration of serum sodium, an increase in output of sodium in the urine and symptoms of adrenal insufficiency follow if the presumptive diagnosis is correct. In the treatment of Addison's disease a low potassium intake (less than 2 gm. per day) has been recommended, although we have been unable to confirm its reported merits in the series of cases in which we are interested.

Recently, an entirely new concept of the value of potassium in Addison's disease has been proposed. If desoxycorticosterone acetate, a synthetic sterol similar to the sterols isolated from the adrenal cortex and useful in the treatment of Addison's disease, is given in excessive amounts it produces an increase in concentration of serum sodium, a decrease in concentration of serum potassium[15] and an exacerbation of malaise, weakness and gastrointestinal symptoms. The effects from overtreatment of patients with Addison's disease are analogous to those of patients with diabetes mellitus who have received an unnecessarily large amount of insulin. Following the assimilation of excessive

quantities of desoxycorticosterone acetate, the level of serum potassium in Addison's disease may decrease to as low as 2.5 milliequiv. per liter. Generalized paralysis of the skeletal musculature may occur, as in periodic paralysis (see below), at this level of serum potassium. For the sake of clarity, it may be reiterated that a high potassium intake is harmful in adrenal insufficiency, but beneficial in patients who have been given inadvertently an excess of the active material during treatment.

Obesity

The use of potassium salts in the treatment of obesity has been recommended by Rusk.[16] It was his experience that a high protein intake supplemented by 4 gm. or more of potassium chloride daily constituted an effective anti-obesity regimen. Undoubtedly the initial loss of weight was associated with the diuretic action of potassium salts. After this effect has passed restriction of caloric intake seems most essential.

Diabetes Mellitus

There are several reports that potassium is associated with assimilation and utilization of carbohydrates in the body. McQuarrie and his associates[17] observed in 4 diabetic children a decreased tolerance to glucose following the ingestion of 12 to 35 gm. of potassium chloride. Gellhorn and Skupa[18] demonstrated that the rate of absorption of glucose from the intestines of frogs is increased by the presence of potassium chloride. Silvette and Britton noted a loss of glycogen from the liver[19] and from the skeletal and heart muscle[20] and an increase of blood sugar following the intraperitoneal injection of potassium acetate. Furthermore, it has been known for more than a decade that a decrease of serum potassium is associated with symptoms of insulin shock. Lastly, in a susceptible person, either an injection of insulin or a high-carbohydrate meal may induce an attack of periodic paralysis with decrease of serum potassium. It may be concluded from these data that potassium has a biological action antagonistic to that of insulin. Clinically, little advantage has been taken of this effect, although McQuarrie et al. have shown that insulin hypoglycemia in diabetes mellitus may be controlled partially with potassium chloride. Further trial of potassium salts in persons difficult to regulate with insulin seems indicated.

Allergic Diseases

Another action of potassium which in many respects is opposite to that mentioned above is its epinephrine-like effect. This has been utilized in the treatment of allergic diseases. Bloom[21] reported beneficial effects in 29 patients with hay fever using 1 or 2 gm. of potassium chloride daily. Many were improved within twenty-four hours, and a few more were improved or completely relieved of symptoms within three days. Bloom recommends daily ingestion of potassium during the entire hay-fever season. Cessation of ingestion may be followed by exacerbations of symptoms. Rackemann[22] has been unable to confirm these findings using similar quantities. He has not abandoned the use of potassium salts, however, and believes that further clinical trial is indicated before making a final commitment. Patients with bronchial asthma do not benefit from potassium chloride so consistently as do those with uncomplicated hay fever.[21]

A discussion of urticaria concludes the allergic manifestations. Rusk and Kenamore[23] treated 6 patients suffering from this disease with an acid-ash diet, high in protein (which is also high in potassium) and low in sodium. In addition, from 4 to 6 gm. of potassium chloride was prescribed daily. All the patients responded to this treatment. Subsequently, a group of 20 patients were treated with similar results. These observations could not be confirmed in 8 patients by Cohen.[24]

Acid-base studies in allergic diseases are few in number, and those which are reported are not complete. Rusk and his associates[25] observed a slight increase above normal in concentrations of serum potassium during exacerbations of bronchial asthma. Clinical improvement was accompanied by a decrease in concentration. At no time was the average range for serum potassium in allergic patients as low as the average range for normals. These authors' interpretation of the higher potassium levels is similar to that advanced by us for Ménière's disease, namely, an elevation in the serum is indicative of a migration of this electrolyte from extravascular areas.

The hypothesis advanced by Bloom[21] in explanation of the beneficial effect of potassium in allergic manifestations was that it participated as an electrolyte in the acid-base balance of the blood. He assumed that the major disturbance was an altered electrolyte metabolism with involvement of the adrenal glands. This explanation is somewhat difficult to accept. One more acceptable to us is an action on the sympathetic synapses or neuromuscular junctions and restoration of vasomotor tone. This is consistent with the data and conclusions of Camp and Higgins.[26] A constriction of the bronchioles induced by histamine could be relieved as promptly and completely by potassium as by epinephrine. They conclude that one function of epinephrine is the maintenance of an optimum potassium level in the body and that changes in potassium are responsible for typical changes ascribed previously to epinephrine.

The objections raised by Engelsher[27] to the treatment of allergic diseases with potassium may be refuted in part. In a series of 64 patients with various allergic manifestations he noted epigastric pain and other intestinal disturbances in a majority. Such symptoms are more likely to develop within a day or two after beginning the regimen. Although he gave no data on the duration of treatment, it is reasonable to believe that his patients took potassium an insufficient length of time to warrant satisfactory conclusions.

Familial Periodic Paralysis

Familial periodic paralysis was one of the first neuromuscular disorders to be treated systematically with a high potassium intake.[28] This malady is characterized by spontaneous attacks of flaccid paralysis of the muscles of the extremities, with a concomitant decrease in serum potassium.[29] The concentration may be as low as 2.5 milliequiv. per liter, a level that may also be reached during paralysis from overtreatment of Addison's disease with desoxycorticosterone acetate. Paralytic seizures have been induced in susceptible persons by injections of epinephrine and of insulin and by ingestion of a high-carbohydrate meal. Each of these procedures causes a diminution in concentration of serum potassium in normal as well as in afflicted persons. The daily ingestion of 2 to 5 gm. of potassium chloride or potassium citrate appears to be effective in preventing paralytic episodes. A boy whom we have been following for more than two years has experienced a marked diminution in the number of attacks per year on such a regimen and is able to live a relatively normal life. The only time he suffers from paralytic attacks at present is after overindulgence in carbohydrates.

The pathogenesis of paralysis of the familial periodic type has not been defined. No change in cholin esterase activity of the serum has been demonstrated. The absolute level of serum potassium appears to be less of a factor in inducing an attack than is a diminution per se in concentration of this constituent. Controlled metabolic experiments have failed to demonstrate a loss of potassium from the body following water diuresis.[30] A migration of potassium from the serum into certain tissues prior to or during the paralytic stage undoubtedly occurs. It is suggested as a hypothesis that the migration is accompanied by a lowering of concentration of potassium in certain synapses of the central nervous system or at the neuromuscular junctions of affected muscles. The prevention and treatment of attacks by potassium ingestion lend weight to this hypothesis.

Myasthenia Gravis

Myasthenia gravis is another neuromuscular disorder which responds in a remarkable manner to the ingestion of potassium.[31] The mechanism of weakness in this disorder is unknown, but it has been suggested that it is associated with an increase of cholin esterase activity at the neuromuscular junction and a diminution of available acetylcholine. Relief from symptoms of weakness is accompanied by restoration of the disordered equilibrium of the chemical mediators at this point.

Potassium chloride was first used in the Massachusetts General Hospital in the treatment of patients with myasthenia gravis in 1936. From 5 to 10 gm. per day was prescribed in addition to prostigmine. Three patients, all severely afflicted, believed that they were improved on this regime. If 5 gm. of potassium chloride was taken simultaneously with 15 mg. of prostigmine, the efficiency of prostigmine was increased and the effect was prolonged. No diminution in the amount of prostigmine required to control the patients' symptoms, however, was observed. In 1937 potassium chloride was recommended to 3 other patients with myasthenia gravis. Benefit was admitted by only 1. The following year the use of potassium chloride was reinvestigated. At that time large amounts were given with striking benefit. The ingestion of 10 to 12 gm., three times a day, in 5 cases was followed by a significant reduction in the amount of prostigmine needed. In patients whose daily requirements were from twenty to thirty prostigmine tablets (15 mg. each) by mouth, it was possible when in the hospital to reduce the number to two or three if large amounts of potassium salts were taken.* A reduction in the cost of treatment and an opportunity to maintain a more complete state of remission were achieved. Up to the present 24 patients have taken or are taking with benefit large amounts of potassium chloride and smaller amounts of prostigmine than formerly.[32] In addition, 7 patients began the ingestion of potassium chloride but discontinued it subsequently, either because they were not helped or because of untoward symptoms. It appears to be impossible to regulate patients on potassium chloride alone. The failure of Minski[33] in the treatment of myasthenia patients with potassium chloride and prostigmine may be attributed to inadequate amounts used.

A satisfactory method for the ingestion of large amounts of potassium chloride embraces the use of

*On the outside, when one is dealing with patients who are of course much more active than a person in a hospital bed all day, no such reduction in prostigmine occurred. In these cases the amount of prostigmine was reduced from twenty to fifteen tablets, and in others from ten to seven, or approximately 20 to 40 per cent.

milk as a vehicle. We have recommended that patients prepare each day a mixture of the following:

Milk	1 quart
Cream	½ cup
Egg	1
Sugar	2 teaspoonfuls
Potassium chloride	8 teaspoonfuls (30 gm.)

The formula may be taken in three divided doses with regular meals. Other patients prefer a 25 per cent aequeous solution of potassium chloride flavored with a small amount of peppermint water. Thirty cubic centimeters of such a mixture may be taken three times a day with meals. Potassium chloride may be prescribed in 1-pound amounts of the dry crystals for the patient to prepare his own solution, or as the 25 per cent solution in large quantities.

Recently it has been observed that a combination of guanidine hydrochloride (0.0125 gm.), potassium chloride (5-10 gm.) and prostigmine (15 mg.) taken with meals gives a sustained effect for three or four hours. Only in most desperate cases is such a combination of anti-myasthenia drugs necessary. It is to be noted that potassium chloride as well as prostigmine and guanidine are potent anti-curare substances.

Ménière's Disease

The history of the use of potassium chloride in the treatment of Ménière's disease or Ménière's symptom-complex seems worth relating. Several years ago Mygind and Dederding[34] assumed that this malady was associated with a disturbance of water and salt metabolism. A waterlogged labyrinth was thought to be at fault and a dehydrating regimen was therefore indicated in treatment. Furstenberg and his associates[35] reinvestigated the problem sometime later, and showed evidence that a retention of sodium was of greater pathogenic significance in the production of symptoms than was a retention of water. They recommended a diet with a low sodium content and the ingestion of ammonium chloride. Since both regimens achieved certain success, it seemed expedient to us[36] to investigate the constituents of the blood before and after treatment. This was done in a group of 33 patients.[37] No increase in concentration of serum sodium was observed during a relapse. This appeared to exclude sodium retention as a significant pathogenic factor in production of symptoms. In 4 patients who were having severe symptoms, however, an increase in concentration of serum potassium was observed. This prompted us to consider several aspects of the regimens which have been recommended and found successful in many patients.

In a diet devised to provide for a low-sodium content, some increase in potassium usually occurs. Since a low-sodium and high-potassium diet was effective, it seemed reasonable to try a normal diet with potassium chloride added. To achieve this, approximately 6 gm. of potassium chloride in an aqueous solution was given daily. No modification of the normal diet was recommended. To date more than 50 patients have been treated in this manner. Most of those who have followed the recommendations have been benefited, although few have been relieved of all symptoms.

Those most severely affected appear to be helped most. Several patients who were having many severe attacks per month have had the incidence reduced to only a few a year. The severity and duration of each attack have been likewise diminished. All except one or two have been able to lead a relatively normal life without the fear of an unexpected incapacitating attack. Several discontinued the daily ingestion of potassium and experienced a return of symptoms after a period of a few days; return to the regimen was followed by a satisfactory alleviation of symptoms. One intelligent but skeptical patient performed this experiment three times before he was convinced of the merits of the high potassium intake. Similar satisfactory results have been reported by Chapman,[38] Graves,[39] Reese[40] and Schneider.[41] Improvement in hearing has been claimed by some patients. We are skeptical concerning this alleviation. With diminution in tinnitus some improvement in hearing would be expected. The precise action of potassium chloride in patients with this syndrome is not known. As a working hypothesis it has been assumed that an increased concentration of serum potassium is indicative of the disruption of normal chemical mediation of impulses in the eighth nerve. Ingestion of potassium may restore normal equilibrium.

Because of the benefit in Ménière's syndrome, potassium salts have been given to patients who complained of one or more symptoms of the classical syndrome, but in whom the clinical picture did not warrant a presumptive diagnosis of this malady. The symptoms complained of included vertigo, tinnitus and deafness. Since potassium chloride is a relatively harmless material, its use seems justified when other forms of therapy are ineffective. The same amounts are recommended as in the treatment of Ménière's syndrome.

Cardiac Disease

Changes in cardiac action with variation in concentration of serum potassium have been reported. Inversion of T_1 and T_2 has been noted[42] in dogs with high serum-potassium levels. In 1930 Wiggers[43] reported alleviation of ventricular fibrillation in dogs following perfusion with a solution of po-

tassium chloride. Sampson and Anderson[44] utilized this observation in human beings in the treatment of auricular and ventricular ectopic beats with tachycardia. In doses of 1 to 16 gm., potassium chloride was effective in restoring normal rhythm in 50 per cent of a small group of patients. It has been suggested that alteration of the electrocardiogram in acute coronary thrombosis[45] may be due in part to alteration in the level of potassium in the muscle.

Untoward Effects

The ill effects of excessive potassium ingestion are believed to be few. Oral administration of as much as 40 gm. per day to patients with myasthenia gravis produced no recognized untoward effects. Gastrointestinal distress usually develops before a toxic amount has been ingested. With onset of gastrointestinal distress assimilation is retarded and excessive quantities are not absorbed. The harmful effects of potassium in untreated Addison's disease have been discussed. Other conditions associated with a diminished concentration of serum sodium and increased concentration of serum potassium, such as heat cramps, acute nephritis, pemphigus and dehydration, might be aggravated. Scudder, Zwemer and Truszkowski[46] called attention to the possible toxic effects of a high serum potassium in acute intestinal obstruction. With the storage of blood and development of blood banks the concentration of the potassium in the transfusion fluid must be considered. If whole blood is stored[47] there is a slow migration of potassium from the blood cells into the plasma. When this concentration exceeds 10 milliequiv. per liter the blood is probably unsuitable for intravenous use in human beings.

Summary

Certain aspects of the role of potassium in the body are reviewed. The action of potassium appears to depend on its effect as an electrolyte, as a substance concerned with carbohydrate metabolism, as an important mediator of the nerve impulse and as a participant in muscle contraction.

In allergic manifestations, Ménière's syndrome and familial periodic paralysis, from 2 to 10 gm. of potassium chloride per day is effective. In myasthenia gravis from 30 to 40 gm. per day may be indicated. In a few conditions a low potassium intake is desirable.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26141

PRESENTATION OF CASE

First Admission. A thirty-four-year-old housewife was admitted to the hospital complaining of vomiting of four days' duration.

The patient had always been well until sixteen years before admission when, at the age of eighteen, she became ill with the following symptoms: ankle edema, dyspnea, palpitation and cough. She had difficulty remembering her sickness. Supposedly the illness lasted about two weeks, and she was then apparently well until eight years before entry when another identical attack occurred. She was then told that she had heart trouble. Some five to six years before entry she had had an attack of tonsillitis, with "occasional" sore throats thereafter. About four years before entry another two-week illness was diagnosed as being due to a "leaking valve." Since that time she had been placed on digitalis, which she did not take regularly. Nine months before admission the patient was injured in an automobile accident, suffering severe bruises, without fractures, to the right chest. She was placed in an outside hospital where the right chest was tapped a few weeks later and a "large amount" of fluid removed, the character of which was not reported. This resulted in some improvement, but she continued to note orthopnea, cough and palpitation, without known ankle edema. After three months' hospitalization she went home and remained in bed, and continued with digitalis. Two weeks before entry she was taken to a summer camp and was moderately active there, but was brought home five days before admission because of dyspnea, palpitation, ankle edema and cough. A physician ordered her to bed and placed her on digitalis, one "pill" every two hours. Instead she took two pills every two hours and began to vomit after having taken ten pills. She vomited every meal thereafter, but continued, nevertheless, to take the digitalis. It appeared that she took a total of 44 gr. in the five days before her admission; it was not known how much was regurgitated. She became quite orthopneic, edema of the legs increased rapidly, and she was alleged to have observed yellow vision but no diarrhea. For about two weeks before admission she occasionally coughed up "bloody" sputum, and she had lost 30 pounds in weight during the ten months before entry.

Physical examination revealed an orthopneic, drowsy, pale, slightly cyanotic, ill-appearing woman, who had a malar flush and distended neck veins and who raised small amounts of bright-red sputum. The heart was enlarged to the left to the region of the anterior axillary line and to the right where its border faded into an area of lung dullness. There was a questionable diastolic apical thrill. The rhythm was grossly irregular; the apex rate was 69, the radial 54. There was a loud heaving impulse. A diastolic murmur was heard at the apex, and a soft blowing diastolic murmur over the aortic area. The pulmonic second sound was accentuated. The blood pressure was 130 systolic, 90 diastolic. The chest was dull up to the angles of the scapulas posteriorly, high in the axillas laterally, and to the fourth ribs anteriorly. The right base was flat. Moist rales were heard in the area of dullness. No rales or breath sounds were heard at the right base. The abdomen was moderately distended with questionable ascites. The liver edge was palpated three fingerbreadths below the costal margin. There was edema of the sacrum, and deep pitting edema of the lower legs. The remainder of the physical examination was negative.

The temperature was 102°F., the pulse 90, and the respirations 30.

Examination of the blood revealed a red-cell count of 4,800,000 with 90 per cent hemoglobin, and a white-cell count of 16,700 with 85 per cent polymorphonuclears. The urine showed a large trace of albumin, and the sediment contained 10 white blood cells, 5 red blood cells and occasional granular and hyaline casts per high-power field. A stool was guaiac negative. A blood Hinton test was negative. The blood nonprotein nitrogen was 44 mg. per 100 cc., the serum protein 6.3 gm., and the icteric index 8 per cent; a direct van den Bergh test was slightly above normal.

Roentgenograms of the chest showed that the diaphragms were unusually high on both sides. The lower portion of the cardiac shadow was obscured by the high diaphragm and by hazy dullness occupying both bases. The heart shadow, however, appeared to be grossly increased in size, both to the right and to the left of the spine. The upper portions of the lung fields were clear. An electrocardiogram taken two days after admission showed auricular fibrillation, with an auricular rate of about 400 and a ventricular rate of about 80. The T-wave changes were consistent with a digitalis effect.

In about three weeks the patient's temperature gradually fell from a daily average of 100 to 101°F. to normal. The apical pulse averaged some 80 to 90 beats a minute, with a radial deficit of 3 to 7 beats. The white-cell count remained elevated around 14,000. A seven-foot film of the heart taken three weeks after admission demonstrated that the greatest enlargement was across the base in the region of the auricles. The pulmonary conus was prominent, and there was an increase in the angle of the bifurcation of the trachea. There were several hazy areas of mottling distributed throughout both lung fields. The right base was clear. Both hilus shadows were grossly increased in width and density, a finding apparently due to venous congestion.

The patient continued to raise decreasing amounts of blood-tinged sputum throughout the hospital stay of seven weeks. She was digitalized, given bed rest and was discharged slightly improved.

Second Admission (almost four years later). The patient had been taking 1½ gr. of digitalis daily and had been fairly well, with only limited activity, until ten weeks before entry, when she developed a head cold. She did not go to bed, and when the cold cleared, she noticed a recurrence of ankle edema, dyspnea, orthopnea and cough. There were no hemoptyses or other symptoms.

Physical examination was essentially unchanged from that of four years previously, except that a late diastolic rumble and early systolic blowing murmur were heard at the apex. An early blowing diastolic murmur at the base was best heard at the second intercostal space on the left. Another examiner found an early diastolic murmur following immediately after the second pulmonic sound (Graham Steele murmur). The red-cell count was 6,500,000 with 112 per cent hemoglobin, and the white-cell count 14,500 with 80 per cent polymorphonuclears. The urine showed a +++ albumin test. Roentgenograms of the chest showed that the heart had a mitral configuration and that there was haziness in the right lower lung field suggestive of multiple small infarcts. Eight days later a portable chest plate showed a small amount of fluid in the right pleural cavity. A definite infarct was not visible. The electrocardiogram was unchanged from the previous admission. The venous pressure was 120 mm. of water.

With bed rest, digitalis and diuretics the patient gradually improved and was discharged on the nineteenth hospital day to a nursing home.

Final Admission (six months later). The patient was not well following her discharge. She had repeated hemoptyses and led a life of invalidism. She was bed-ridden for six weeks before her final admission. Nausea and vomiting were relieved five days before entry by omitting digitalis, but her edema increased. It was stated that she had always had an abnormal tendency to bruise easily, but it had become more marked. Mottling appeared over her arms and legs, and large confluent black-and-blue ecchymoses on her fingertips and toes; these were sensitive at first. There had been no pain in the left upper quadrant of the abdomen. She had, however, passed "red" urine during the week before entry, so much so that she wondered if her menses had not begun.

Physical examination revealed an apathetic woman who appeared gravely ill. The malar flush was prominent and was purplish. There were many splinter hemorrhages and large ecchymotic areas on the tips of the fingers and toes, together with mottling of the extremities. The entire body, including the face, eyelids and arms, was waterlogged. The breath was foul but not uremic. The neck veins were distended, and yet the patient was able to lie flat in apparent comfort. The chest was almost clear of rales, but there were signs of fluid on the right. The heart was as previously described except that there was a grossly irregular but fairly consistent bigeminal and occasionally trigeminal rhythm, with a pulse deficit of 40 and a soft mid-diastolic murmur maximal at the pulmonic area and transmitted down the left border of the sternum. The pulmonic second sound was much louder than the aortic. The blood pressure was 140 systolic, 80 diastolic. The liver was just palpable, and the abdominal wall was so edematous that further examination was impossible.

The temperature was 100.2°F., the pulse at the wrist 86, and the respirations 20.

The blood showed a red-cell count of 6,600,000 with 125 per cent hemoglobin, and a white-cell count of 20,800 with 84 per cent polymorphonuclears. The color index was 1.05, and the mean corpuscular volume 100. The urine showed a ++++ albumin test, and the sediment contained 5 to 6 red cells and innumerable white cells per high-power field. The serum non-protein nitrogen was 78 mg. per 100 cc. The hematocrit was 65, the uncorrected sedimentation rate 0.2 mm. per minute, the blood clotting time 10 minutes, the bleeding time 1.5 minutes, and the clot retraction normal. The venous pressure was 170 mm. of water. An electrocardiogram showed low T_1 and T_2 and inverted T_3; Q_3 was 7 mm.; there were runs of bigeminal rhythm and auricular fibrillation, with ventricular premature beats.

On admission the patient appeared to be in terminus, but following treatment with Salyrgan and omission of digitalis she rallied for a time. The temperature ranged upward to 100 or 101°F. daily, and although she had sufficient diuresis, she failed

gradually and went into a state of peripheral vascular collapse with icy extremities, impalpable pulse, absent blood pressure, extreme cyanosis, dyspnea and profuse sweating. She was placed in an oxygen tent, but died on the twentieth hospital day.

Differential Diagnosis

Dr. T. Duckett Jones: It is very interesting that ankle edema, dyspnea, palpitation and cough are frequently repeated throughout the record, and it is fair to assume that at the age of eighteen the patient had congestive heart failure. I also should be willing to suggest in view of the absence of a previous history of heart disease that she had rheumatic heart disease and had insidiously developed mitral stenosis. It is further suggested that active rheumatic fever was probably responsible for the congestive failure.

At the age of twenty-six she again had what seems to be a mild episode of congestive failure, probably again on the basis of acute rheumatic fever. At thirty she had another episode and valvular heart disease was diagnosed. Auricular fibrillation may have begun at this time, but I should doubt it because of the subsequent events.

Following the automobile accident, she had a long period of illness with weakness and congestive failure, and I presume that the right chest fluid was either the fluid of congestive failure or of pleuritis coincidental with active rheumatic fever. Whether the accident had anything to do with precipitating the rheumatic fever is problematical, but we have seen a good many cases in which there was an apparent association between an operation, accident or non-streptococcal event and recurring rheumatic fever.

Apparently she had digitalis intoxication, although there seems to be some doubt as to the actual amount of the drug which the patient retained.

It is obvious that for almost a year prior to admission to the hospital she had had some active disease process which resulted in a great deal of weight loss, and it is possible that the accident increased the symptomatology. We are not certain, however, of the actual existence of symptoms prior to that time. It is possible also that auricular fibrillation may have started shortly after the accident and that its onset began the gradual downhill progress.

The distended neck veins and bright-red sputum suggest that she may have had a pulmonary infarct or infarcts.

Apical thrill is not common in rheumatic heart disease with auricular fibrillation for obvious reasons.

The accented pulmonic second sound is probably indicative of mitral stenosis.

The patient had slight fever and perfectly good evidence of an active disease process. Congestive failure was present in a patient with probable mitral and aortic disease, and there was nothing very unusual about the picture as presented at the time of the first admission.

The negative Hinton test is of interest in view of the differential diagnosis to be discussed later. I regret that there was no venous pressure recording on the first admission. It might be of some help in clarifying the subsequent events.

The sedimentation rate was not determined, but this would not have been helpful in view of the presence of a large liver.

"The pulmonary conus was prominent, and there was an increase in the angle of the bifurcation of the trachea." She probably had quite large auricles, and conspicuous enlargement near the base of the heart would probably account for this x-ray finding.

"There were several hazy areas of mottling distributed throughout both lung fields." This is in keeping with pulmonary infarcts or pulmonary changes seen at times during rheumatic fever.

Seven weeks is a very long period for a patient with ordinary congestive failure to have hemoptysis. She did not have spells of severe orthopnea with pulmonary edema, which are common in the patients with mitral stenosis who have hemoptysis. Apparently she improved slowly, despite the fact that during her few weeks' stay in the hospital she had evidence of something continuously going on in the lungs in addition to the picture of congestive heart failure. The symptomatology was very much the same as that of her earlier bouts of congestive failure.

Physical examination at the time of the second admission, nearly four years later, showed a decided change in the patient. The description of a Graham Steele murmur raises a question of considerable interest because such murmurs are rare, and one wonders if we are justified in making such a diagnosis unless congestive heart failure was present. It may be possible that this patient had two diastolic murmurs of very similar quality at the base of the heart.

The red-cell count was 6,500,000 with 112 per cent hemoglobin, and the white-cell count 14,500 with 80 per cent polymorphonuclears. This is the first time we have noted any evidence of polycythemia. The white count may be explained entirely on the basis of the polycythemia.

I do not know the extent of the peripheral edema, but I notice in the treatment that the patient received diuretics as well as digitalis. The

question might be raised as to why she developed such a high red-cell count. This polycythemic tendency was not very pronounced at the time of this admission. Apparently the tendency increased considerably in the six months between the second and the third or final admission. I think we can assume that the patient had pulmonary infarcts or something by x-ray which was very suggestive of pulmonary thrombosis. There had been a change in the clinical picture, and the pulmonary system began to assume a more and more important role. The cyanosis was very striking. Extensive cyanosis and ecchymotic areas over the tips of the fingers and toes are suggestive of extensive pulmonary changes and probably alteration of the minute peripheral vessels.

"The neck veins were distended, and yet the patient was able to lie flat in apparent comfort." That is a striking feature. I presume the venous distention was noted with the patient sitting erect. Such a combination is most unusual. There was obviously no extensive left-sided cardiac failure, because such patients are not able to lie flat comfortably. In children with rheumatic disease and cardiac failure one often sees right-sided heart failure, with high venous pressure, edema of the face, a large liver and peripheral edema. The lungs remain remarkably clear and the patient often prefers to lie flat. This is rarely seen in adults. In this patient there was little or no elevation of the venous pressure, and despite the lung changes the patient could lie flat. This strongly suggests that the pulmonary changes were not the result of ordinary congestive heart failure (left-sided failure).

". . . a soft mid-diastolic murmur maximal at the pulmonic area and transmitted down the left border of the sternum." This again could denote either an aortic diastolic murmur or the Graham Steele murmur of relative pulmonary insufficiency. The pulmonary second sound was louder than the aortic second sound. The patient had mitral stenosis and hence might have a good reason for an accentuated pulmonic second sound, but that is a helpful feature of the differential diagnosis that I shall give a little later.

"The liver was just palpable." This is another finding which suggests little, if any, right-sided heart failure. Large painful livers are often an outstanding feature of failure of the right side of the heart.

Apparently she did not have a palpable spleen at any time. The blood examination still showed a definite polycythemia, with perhaps infection as indicated by the increase in polymorphonuclears. I should doubt any serious alteration in the blood-forming organs.

The hematocrit was 65, in keeping with the polycythemia. There was abundant evidence that the patient did not have thrombocytopenic purpura. There was a distinct increase in retention of the nonprotein nitrogen since the preceding admission. A level of 78 mg. per 100 cc. is fairly high for a patient with ordinary congestive failure.

"The venous pressure was 170 mm. of water." That is not very high. I suppose it is an indication of some degree of congestive failure, especially of the right side of the heart, but there is considerable variation in venous-pressure technics. I am not familiar with the exact routine used in the medical wards, but with probably the same method, we usually observe tremendous increases in venous pressure even long before evidence of peripheral edema. Here was a liver that was but little enlarged, and a patient who could lie flat in bed. I should presume on the basis of these facts that congestive heart failure was not severe.

Dr. White will probably mention the electrocardiogram because it offers suggestive evidence of the presence of pulmonary infarction. Also the probability of pulmonary hypertension comes into play because of the finding of a very strong pulmonic second sound and the persistent hemoptysis. The story and findings fit in with massive pulmonary infarction or thrombosis.

This is an exceedingly difficult differential diagnosis. It is not the usual problem met in cases of rheumatic fever and heart disease. The first few years are in keeping with those of a patient who has developed insidious rheumatic heart disease and probably repetitive bouts of congestive heart failure. It is safe to assume that she had rheumatic heart disease, mitral stenosis with auricular fibrillation, probably mild aortic disease and, possibly, pulmonary disease. These features, however, do not explain the patient's death. In other words, I do not believe she died as a result of either rheumatic heart disease per se or of acute rheumatic fever in the ordinary sense of fulminating rheumatic fever. There are some features difficult to explain, for instance the massive edema and the relatively little evidence of nephritis. The retention of nonprotein nitrogen and the urinary findings hardly explain the death on the basis of acute glomerulonephritis, so I think we must try to explain the syndrome largely on the basis of a disease or change in the blood vessels.

The first thing that comes to my mind is periarteritis nodosa. She had many of the features of this disease, but not all of them; and the blood picture is distinctly contrary to the usual finding. We know that in such cases 80 per cent may show renal changes. No peripheral nodes were noted. I should say that the chief feature against peri-

arteritis nodosa is the fact that there was not enough evidence of arterial change in various locations. In periarteritis nodosa the large vessels are not usually involved; in this patient, apparently there were changes in the large vessels of the pulmonary tree. In addition, there have been some extraordinary pulmonary specimens reported in which extensive arterial nodules occurred in the lung tissue, without appreciable alteration in the pulmonary circulation.

I think the advanced edema was not entirely the result of congestive heart failure, but to some extent probably dependent on hypoprotinemia. There is no mention of the serum protein during the last illness.

At the end the patient presented a picture much like Ayerza's disease. That, as you know, is supposed to be syphilitic in origin, but we have no evidence in this patient of a syphilitic process. There have been a small number of pathologists who have constantly written about pulmonary changes in rheumatic fever of an arterial nature. Four years ago Parker and Weiss[1] reported a case which, except for two features, was very similar to this one. Their patient had pulmonary edema in increasingly severe episodes and died, but did not have massive peripheral edema. Gouley[2] and his co-workers in Philadelphia have written repeatedly about pulmonary fibrosis and changes that occur in rheumatic fever and have stated that the reason for failure of the right side of the heart is often the result of pulmonary change. We have seen very little of this in gross pathological specimens and no real syndrome clinically. However, Cash,[3] at the University of Virginia, has been impressed with the great frequency with which you get intimal changes in moderate-sized and small-sized blood vessels in patients with rheumatic fever, particularly in those who have had the disease over a period of years. The case Parker and Weiss described had extensive changes in the fair-sized arteries of the lungs and in the small arterioles. They compared this change with that which is found in malignant nephrosclerosis, and I think it is fairly obvious that this patient must have had some change in the blood vessels of the lung over a fairly long period of time. She probably had hypertension of the pulmonary circulation and coexistent changes in the blood vessels in other parts of the body. Changes in the pulmonary vessels were probably responsible for the rather progressive nature of the disease and for the fatal outcome. Whether it can be said that she was suffering from chronic cor pulmonale I do not know. Ayerza's disease is of course very much of this nature, but I do not believe that the patient had this type of change. However, she did not present the syndrome of acute cor pulmonale with a rapidly terminal course. The chronicity of the process is somewhat against ordinary pulmonary infarction or thrombosis as the cause of the whole difficulty. I think she would have died much sooner with a less severe generalized disease process if this had been true. The picture, as I see it, is probably one of pulmonary arterial disease, possibly on a rheumatic basis. Of the latter I am not sure, but I should say that the process was not limited to the pulmonary arteries but extended throughout the body, although the changes were more pronounced in the lung and kidneys.

Dr. Frederick T. Lord: Was a blood culture taken?

Dr. Tracy B. Mallory: I can find no record of it.

Dr. Lord: The picture suggests that she might have had right-sided endocarditis with pieces breaking off and going into the lungs.

Dr. Edward F. Bland: The x-rays are not here, but I should like to raise the question of a possible complicating interauricular septal defect plus the mitral stenosis. It would be difficult to make this diagnosis without seeing the films and the electrocardiogram. This combination may give a curious x-ray picture with especially prominent lung changes. I should like to ask Dr. Jones if he would want to consider that combination here.

Dr. Jones: I think it is possible but there is no real evidence to support the diagnosis. This whole thing could be explained on the basis of a congenital defect in addition to mitral stenosis, but there is no early story suggesting a congenital defect, and the age of the patient is somewhat against such an association of lesions over a period of at least sixteen years. I thought very seriously of whether something could have developed in the nature of an arteriovenous aneurysm, but there is no evidence to support such a diagnosis. It is possible that such a shunt may have had something to do with the picture.

Dr. Paul D. White: Dr. Jones has done extremely well. Have we the electrocardiogram? It would be of value in determining whether an interauricular septal defect was present. I find that the angle of the axis is only 90°. The only cases of congenital auricular septal defects that we have followed through have had marked right-axis deviation (110° or more). This finding is against the diagnosis of auricular septal defect. The electrocardiogram, to be sure, does show rather large Q waves in Leads 2 and 3, which may be explained on the basis of any factor causing enlargement of the right ventricle. It is possibly the result

of a cor pulmonale of the acute, subacute or chronic type. But the record is not clear-cut, perhaps due to a combination of factors.

Some of the events that had happened in the past were probably episodes of pulmonary infarction. We know that such infarcts can occur in acute rheumatic disease as well as from embolism of whatever cause.

I do not know whether my auscultatory findings were accepted by those who wrote up the record; they are not mentioned here. It intrigued me on the wards a few days before she died that there was a striking diastolic rumble close to the left border of the sternum at its lower end, which was almost as marked as any that I have heard at the apex in mitral stenosis. She had not shown this a year or two before, as we found out by looking back through the outpatient record. It was a murmur that made one think strongly of tricuspid stenosis. It followed a very loud, blowing, early diastolic murmur heard in the pulmonic-valve area. There was no doubt about the pulmonary diastolic murmur being a Graham Steele murmur; it was very loud and heard maximally in the pulmonic-valve area after a very loud second sound. I thought there were three separate murmurs, namely those due to mitral stenosis and to pulmonary regurgitation and something that resembled the murmur of tricuspid stenosis. I do not know whether we suggested the possibility of a right-sided Austin-Flint murmur then, but that came up later.

The final point that interested us was the condition of the fingers and toes (mottling and ecchymoses) and the very marked cyanosis; it made us think of a ball thrombus in one auricle or the other. Because of the novelty of the case we suggested that it might be in the right rather than in the left auricle, but that was a wild guess.

Clinical Diagnoses

Rheumatic heart disease, with mitral stenosis.
Tricuspid stenosis, with auricular fibrillation?
Congestive failure.
Pulmonary infarction.
Compensatory polycythemia.

Dr. Jones's Diagnoses

Rheumatic heart disease.
Mitral stenosis.
Auricular fibrillation.
Congestive failure.
Compensatory polycythemia.
Arterial thrombosis or fibrosis, pulmonary and renal (? rheumatic).

Anatomical Diagnoses

Rheumatic heart disease, chronic, with mitral stenosis.
Endocarditis, acute rheumatic, aortic, mitral and tricuspid.
Cardiac hypertrophy and dilatation.
Thrombosis of left pulmonary artery.
Thrombosis, massive, of left auricle.
Thrombosis, left renal artery, abdominal aorta and common iliac arteries.
Pulmonary infarcts, healed.
Renal infarcts, fresh and healed.
Anasarca.

Pathological Discussion

Dr. Mallory: This was obviously a most complicated clinical picture, and the autopsy findings were equally complicated and numerous. The primary underlying condition was rheumatic heart disease with mitral stenosis. The degree of mitral stenosis, however, was not severe. The circumference of the valve was 5 cm. so that on anatomical grounds under ordinary conditions one would not expect a heart to fail this rapidly. This valve and the aortic and tricuspid valves all showed small pin-point vegetations suggestive of acute rheumatic involvement. We found nothing to suggest bacterial endocarditis. The right side of the heart was very markedly dilated, both auricle and ventricle, and there was considerable bulging of the pulmonary conus, a very characteristic finding in cor pulmonale. The main pulmonary artery was also markedly dilated, and the major branch of the left lung was almost completely occluded by old organized thrombus. The branch to the upper lobe was totally occluded, that to the lower lobe almost completely occluded. There were also several depressed scars on the pleural surface, which on lengthy investigation in the hands of Dr. Castleman were eventually proved to be healed infarcts. There was one fresh pulmonary infarct, 7 cm. in diameter, in the other lung, not a strikingly large one and not adequate to explain the sudden death.

Another peculiar finding which may possibly have had functional significance was an enormous thrombus in the left auricle which was so large that only a small lumen, a little over 2 cm. in diameter, was left. The mouths of the pulmonary veins were impinged on by this thrombus, and it was difficult to understand how the blood got back from one lung.

The other major finding was in the systemic circulation where a large thrombus was found beginning just below the diaphragm in the abdominal aorta and extending all the way down into the iliac arteries. The degree of narrowing varied from one to two thirds of the diameter. It overlay the mouth of the left renal artery, and the

thrombus extended out into the small intrarenal branches. This and the aortic thrombus were obviously old, being completely organized; the left kidney had shrunk to 25 gm. in weight but what remained of the kidney tissue was viable. On the right there was fresh infarction of the major part of the kidney, so I should think there must have been a considerable element of uremia in the picture. Whether it was enough in itself to have caused death, I am not sure. For the dramatic terminal episode I have no explanation. We did not have permission to examine the head. Conceivably something there might have been responsible for it.

DR. WHITE: May I add one further comment about the mid-diastolic murmur in the tricuspid-valve area? In the absence of tricuspid stenosis it should be regarded, I think, as right-sided Austin-Flint murmur.

DR. JONES: What about the blood vessels in the lungs?

DR. MALLORY: I could see nothing in them that I could recognize as a specific arteritis. The larger vessels showed obliteration, which I interpreted as the result of organization of thrombi. The small arteries of the lungs did show diffuse thickening of the walls of the type Parker and Weiss described; this condition was extensive and no doubt contributed to the picture.

DR. HOWARD B. SPRAGUE: Is this a case of partial renal ischemia without hypertension?

DR. MALLORY: We have seen so many that I did not remark about it.

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CASE 26142

PRESENTATION OF CASE

A thirty-two-year-old American dye-machine operator entered complaining of numbness of the left leg.

Three months before entry he noticed numbness in his left foot. This condition gradually spread up the leg to the thigh and finally to the abdomen. He noticed that the numbness stopped exactly in the mid-line. During the following two months the left chest and arm gradually became involved. The numbness was described as an inability to appreciate pain or to feel things as well as usual. He was unable to distinguish hot from cold but noted that hot water produced a burning sensation which was quite unpleasant and painful. He also noticed that the right side of his face felt numb while shaving. Two months before entry his voice became weak toward the end of the day and he was unable to produce any sound. He began having attacks of hiccups, usually about 10:00 a.m. These were relieved by drinking cold water. One month before entry he noticed difficulty in swallowing. Solid food seemed to "stick" in his throat. Approximately two months before entry he developed unsteadiness of gait, characterized by deviation to the right, so much so that his friends thought he was intoxicated. During the month before entry he developed right occipital headaches just above the mastoid. These headaches often spread throughout his head. There was no history of tinnitus, dizziness, vomiting, aphasia, or blurring or double vision. These symptoms as they developed lasted until admission, with no improvement.

His family and past histories were noncontributory. He had been married eight years. His wife and two children were living and well. There had been no miscarriages.

Physical examination showed a well-developed and well-nourished man in no acute distress. Except for a few slightly enlarged axillary and inguinal nodes the examination was negative. The blood pressure was 135 systolic, 85 diastolic.

A neurological examination gave the following positive findings. There was loss of pain and temperature sensations on the left side of the body; touch and vibration sensations everywhere were normal. The right pupil was slightly smaller than the left. There was rotary nystagmus. The corneal reflex was absent on the right and active on the left. The hearing was normal. Air conduction was greater than bone conduction. The Weber test was not lateralized. The palate was deviated to the left, and the gag reflex on the right was diminished. There was a questionable weakness of the right side of the tongue. When standing he deviated to the right almost constantly. His tendon reflexes were all active and equal on both sides. The abdominal and plantar reflexes were normal.

The temperature was 98°F., the pulse 76, and the respirations 20.

Examination of the urine was negative. The red-blood-cell count was 5,660,000, with a hemoglobin of 100 per cent. The white-blood-cell count was 7400, with 79 per cent polymorphonuclears. A blood Hinton test was negative. On lumbar puncture 15 cc. of clear colorless fluid was withdrawn. The initial pressure was 145 mm. of water; the pressure rose to 300 mm. on jugular compression and immediately fell to its previous level on release. An alcohol test was positive, and an am-

monium sulfate test negative; no cells were found. The total protein was 38 mg. per 100 cc.; the gold-sol and Wassermann tests were negative.

During the first four days in the hospital he developed nausea, vomiting and increased difficulty in talking and swallowing. He also complained of considerable dizziness, which was partially relieved by lying on his right side. The impairment of pain and temperature sensations gradually spread and involved the left face, as well as the right face and left side of the body. There was considerable nystagmus, although the eyes moved well. His hearing remained normal. During the second and third weeks he was treated with six small doses of x-rays. His symptoms improved somewhat, although none of the important signs which were present on admission entirely disappeared. At the time of discharge from the hospital, during the fourth week, he had slight hypesthesia of the right side of the face but no facial weakness. The nystagmus to the left and the unsteadiness of his right arm and leg had diminished, also the vomiting and hiccups. There was slight but definite improvement in the ability to recognize changes of temperature on the left side. On the other hand, fibrillations and atrophy of the right half of the tongue, signs which were not present on admission, developed during his stay in the hospital.

While at home he continued to improve subjectively. An examination performed by his physician one month after discharge showed marked weakness of the right arm and leg not limited to any muscle group. The uvula deviated slightly to the left. He complained of marked right occipitoparietal headaches. During the following month there was much more marked subjective improvement. The headaches disappeared almost completely, and his walking improved to the extent that he was able to go downstairs without help. His appetite was good, and there was an evident gain in weight. There was only an occasional hiccup. Examination two months after discharge showed slight nystagmus. There was no definite facial weakness, but wrinkling of the forehead was perhaps slightly less on the right than on the left. The uvula was in the midline but deviated to the left with phonation. Sensory impairment similar to that described above persisted. Position sense was normal. The reflexes were active and equal. There was considerable staggering on walking.

During the third month after discharge from the hospital his walking became progressively worse, his headaches returned and he became decidedly depressed mentally. He threatened suicide and on the day before death, exactly three months after discharge from the hospital, attempted to hang himself. He was admitted to a hospital where he received sedatives. That evening his respirations decreased and his pulse could not be felt. One hour later he developed sudden respiratory paralysis and died.

Differential Diagnosis

Dr. Raymond D. Adams: The initial complaint, that of numbness of the left leg, is readily explained by the finding of hypalgesia and thermohypesthesia, both of which are signs of a lesion involving the lateral spinothalamic tract. The progression of the numbness from leg to trunk and upper extremity is possible because of the lamination of the fibers within the lateral spinothalamic tract, the leg fibers which are most lateral being involved first. I do not know how to interpret the unpleasant burning sensations. Since there was no sensory disturbance over the left side of the face, the lesion of lateral spinothalamic tract must have been in the medulla or pons below the point where the ventral trigeminal lemniscus joins the lateral spinothalamic tract. The loss of pain and temperature sensations on the right side of the face and the absent right corneal reflex mean involvement of the spinal tract and the nucleus of the trigeminal nerve. Again this involvement must have been between the mid-pons and medulla oblongata to account for all the divisions of the trigeminal nerve that were affected. This crossed sensory disturbance places the lesion in the medulla or pons on the right side.

The next developments — dysphonia, dysphagia, the absent right gag reflex and palatal deviation to the left — signify involvement of the right nucleus ambiguus, which lies just medial to the lateral spinothalamic tract. Singultus is a respiratory reflex and undoubtedly of central origin in this case, presumably from a disturbance in some of the connections of vagus nerve, such as the nucleus of the tractus solitarius or the nucleus intercalatus. These additional findings locate the lesion in the medulla, more specifically in the retro-olivary region.

Unsteadiness of gait with deviation to the right and inco-ordination of movements of the right arm and leg are cerebellar signs. In this case they were probably due to interruption of the right spinocerebellar tracts. The tracts are just lateral and dorsal to the lateral spinothalamic tract, the spinal nucleus and the tract of the trigeminal nerve.

Slight miosis of the right pupil was observed, but the other components of Horner's syndrome are not mentioned. Pupillodilator fibers from the hypothalamus to the cervical spinal cord (descending sympathetic tract) pass through the reticular

substance of the medulla very close to where the lesion appears to have been. This tract is uncrossed, hence the ipsilateral sign.

Nausea, vomiting and vertigo, without tinnitus or deafness, can only mean a central vestibular disturbance. The spinal vestibular nucleus and its connection with the dorsal motor nucleus of the vagus afford a ready explanation of these symptoms. The rotary nystagmus is on this basis.

The loss of pain and temperature sensations on the left side of the face makes us think of a lesion of the ventral trigeminal lemniscus tract after it has crossed. This tract originates in the nucleus of the spinal tract of the trigeminal nerve and decussates almost immediately, coming to lie along the ventromedial portion of the medial lemniscus; in the upper pons it joins the lateral spinothalamic tract and continues to the ventral nucleus of the thalamus. Thus, the lesion extended medially and interrupted this tract after it had decussated.

Another indication of a medial extension of the lesion was the atrophy and fibrillation of the tongue. This is caused either by destruction of the right hypoglossal nucleus or the fibers of this nucleus as they course ventrally toward the pyramidal tract.

The weakness of the right arm and leg, which was observed only once and then without reflex changes, I shall place in the group of cerebellar signs; there is no evidence of pyramidal-tract disease. The facial weakness was too uncertain to consider seriously. The depressed mood which led to his suicidal attempt I cannot put on a neurological basis. Lesions of the posterior hypothalamus are associated sometimes with apathy, drowsiness and depression, but here it is safer to consider the depression as a reaction to an incurable disease. The right occipital headaches confirm the lateralization, which is well established; they are not a sign of increased intracranial pressure.

From these data I think we can be sure of a single lesion in the right tegmentum of the medulla oblongata at about the level of the olive, involving, in order, the lateral spinothalamic tract, the spinal nucleus and tract of the trigeminal nerve, the nucleus ambiguus, the dorsal and ventral spinocerebellar tracts, the nucleus solitarius and its tract, the spinal vestibular nucleus, the dorsal motor nucleus of the vagus nerve, the ventral trigeminal lemniscus and the hypoglossal nucleus.

There occur to me five possible causes of such a lesion. An occlusion of the right vertebral and right posteroinferior cerebellar artery produces a retro-olivary syndrome. The gradual onset and progression of symptoms is unlike a vascular lesion, due either to hemorrhage or to thrombosis. Also the lingual atrophy and the loss of pain and temperature fibers from the opposite side of the face are not parts of this syndrome, so more than one vessel would have to be occluded.

Tuberculoma must always be considered in a progressive lesion of the medulla, pons or cerebellum. There is not sufficient positive information, such as signs of pulmonary tuberculosis, fever and leukocytosis, on which to make such a diagnosis, but it cannot be excluded.

Syringobulbia is a diagnosis which must be mentioned in passing, chiefly because it sometimes produces lesions in this region of the central nervous system. However, rapid progress of the lesion and an early fatal termination are unusual, and the lesion in this case appears to be too discrete. I cannot dismiss this diagnosis with certainty but consider it less likely than those which follow.

Acute multiple sclerosis or encephalomyelitis, a disease entity which most neuropathologists prefer to separate from ordinary multiple sclerosis, is a possibility. However, the onset of symptoms and signs is more acute and the remissions are more certain than any which were found in this case. Particular attention is called to the statement that although there was improvement in some of the signs none of the important ones ever disappeared. If a single sign had completely cleared up, even after roentgen therapy, we should probably have to consider acute multiple sclerosis as the most likely diagnosis. The fact that the signs point to a solitary lesion and not to disseminate ones is also against this diagnosis.

The most probable cause of this clinical picture is an intramedullary glioma. The insidious onset, the slow progression of symptoms, and the manner in which adjacent tracts and nuclei were involved all favor this diagnosis. As to the type of tumor, we can only guess; spongioblastoma multiforme, spongioblastoma polare and astrocytoma are the commonest. We have no reason to suspect a lymphoma or a metastasis of a tumor elsewhere in the body. The laboratory data are of no help. Evidently the attending physician also diagnosed tumor and prescribed x-ray treatment. Signs of increased intracranial pressure occur late in brain-stem tumors and are not necessary for the diagnosis of a tumor of the medulla.

The patient died of respiratory failure. Whether the hanging or the sedation were contributory factors I cannot say; the lesion itself probably was sufficient.

Clinical Diagnosis

Encephalomyelitis?

Dr. Adams's Diagnosis

Glioma of right tegmentum of medulla oblongata.

Anatomical Diagnosis

Glioblastoma multiforme of medulla.

Pathological Discussion

Dr. Charles S. Kubik: Dr. Adams has made a very good analysis of the symptoms and findings, and his diagnosis is correct both as to the nature of the lesion and its localization. There was a diffusely infiltrating glioma of the right side of the medulla. It measured from 3 to 4 cm. in diameter and involved the whole of the right side dorsal to the inferior olive. It apparently did not extend beyond the midline or into the pons. Microscopically it was a glioblastoma multiforme. The case is rather unusual in that the tumor was restricted to the medulla. Most of the gliomas of the brain stem involve the pons or the pons and midbrain. These too may be, and often are, limited to only one side of the brain stem.

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EDUCATIONAL QUALIFICATIONS FOR HEALTH OFFICERS

The Committee on Professional Education of the American Public Health Association has recently issued a report* in which it discusses the educational background desirable in the training of health officers. The difficulties encountered by this committee must be very like those encountered by the "boards" of the various specialties. It is not easy to maintain a balance between the practices of the past and the theories of the future. In the same breath that they state the optimal educational advantages which should be insisted on they must also admit that the optimal performance at which they aim has been repeatedly achieved by individuals whose educational advantages were deficient if measured by the standards they wish to promulgate. The result is that such committees and boards must tread lightly until they have established themselves and their principles.

In the field of public health it would seem that a few major principles have been established. The first recommendation of the committee is as follows: "That candidates for appointment as health officer should be graduates of approved medical schools who have completed successfully not less than one year of internship in an approved hospital and in addition a course of not less than one year of graduate instruction in a university, leading to a degree in public health." From this it would seem that the medical degree has been accepted as a necessary possession for all who covet a recognized career in public health. This is a significant decision because the field is occupied by a large number of associated professions. It expresses the belief that public health cannot be effectively administered by those who do not understand the language of the medical profession. The same is already true in other fields, such as those of hospital administration, industrial health and the trained varieties of social service.

Thus in many fields the degree of Doctor of Medicine may be utilized as a preliminary attainment beyond which the individual fully intends and is expected to narrow himself into a more limited proficiency. Recently a twenty-six-year-old nurse anesthetist embarked on a ten-year program in order that she might become an anesthesiologist. It is sometimes difficult to know whether our educational systems are preparing their votaries to serve themselves or their fellow men and women, or perhaps they are already too vast to be anything more than gigantic information bureaus. The best of them graduate relatively inexperienced individuals, and this is covered by the second recommendation: "That recognition be given to the fact that practical experience in public-health administration is an essential part of the education of a health officer. . . ."

A committee formed by the Massachusetts Central Health Council to make inquiry into this subject has recently reported similar difficulties in

*The educational qualifications of health officers. *Am. J. Pub. Health* 29:1342, 1939.

framing suitable standards. This committee however, did uncover a law in Connecticut that requires that county health officers be lawyers! While it is doubtful that public-health law is as yet sufficiently involved to make this a wise requirement, if this or any other provision might ensure good administrative ability on the part of the officer it would, to that extent, have merit. Whereas a competent administrator can readily get technical advice, a competent technician needs more than advice to do a good administrative job.

The superior health officer, anesthetist, hospital superintendent or anyone else will remain the person whose graciousness, personality and intuitive appreciation of what is fitting on all occasions equal or surpass his knowledge of mere technics.

ADVANCES IN CANCER CONTROL

The American Society for the Control of Cancer and its managing director, Dr. Clarence C. Little, deserve congratulations for the pamphlet* issued by the Public Affairs Committee, entitled *The Fight on Cancer*. It is short and readable, with graphic presentation of figures. The one point that might be objected to is the all too frequent error of overestimating the curability of skin cancer. The familiar figure of 95-per-cent curability in early cancer as against 30-per-cent curability late in the disease is given, whereas careful analysis of large series shows that even in very favorable lesions, and omitting such forms as malignant melanoma, only a little over 90 per cent are curable, and in taking advanced cases, 20-per-cent curability is perhaps a generous estimate.

The section on research in cancer is very clear and useful. One of the most important phases of cancer investigation — the field of radiation therapy — is, perhaps wisely, not touched on in this pamphlet. In Boston, thanks to the efforts of the pioneer radiologists and their successors of the present day, together with an unparalleled cooperation of the departments of physics and of chemistry of Harvard University and the Massachusetts Institute of Technology with the various cancer investigation and treatment centers, there has developed an armamentarium for the study of the efficacy of radiation therapy that is duplicated nowhere else in the world. With x-ray apparatus ranging from the ordinary therapeutic types through machines of 400,000 to 1,000,000 volts in constant use, with a 3,000,000-volt x-ray machine approaching completion at the Massachusetts Institute of Technology, with an adequate supply of radium and radon, with practically unlimited opportunity for the making of temporarily radioactive compounds through the two great cyclotrons at Harvard University and the Massachusetts Institute of Technology, there is an ideal situation for the development of knowledge along these lines. If radiation therapy does not make great strides in the control of cancer in the next few years, it will not be for lack of personnel or equipment, at least in Boston.

*Little, C. C.: The fight on cancer. *Public Affairs Pamphlets*. No. 38. 31 pp. New York: American Society for the Control of Cancer, 1939.

MEDICAL EPONYM

Blaud's Pill

Paul Blaud (1774–1858), chief physician of the hospital at Beaucaire and corresponding member of the Royal Academy of Medicine of France, is chiefly remembered for his famous pill, the formula of which was given in an article presented to the Royal Academy of Medicine, August 23, 1831, entitled "Memoire sur les maladies chlorotiques, et sur un mode de traitement spécifique dans ces affections [An essay on the chlorotic affections and a specific method of treatment]." This appears in the *Revue médicale* (1: 337–367, 1832). A portion of the translation follows:

> Iron has always been used in chlorosis, for which it has been considered a specific; but all practitioners know how uncertain is its effect in this disease, and how often it fails; *a failure which results from the feeble doses administered, and from the fact that it is given in an unsuitable form*. . . . Modify the iron with regard to the absorbent capacity of the intestines, and, secondly, administer it in a sufficient dose. All the conditions will then be present for its action on the organism, and the effects of this precious metal will be quickly manifest.
>
> The following formula fulfills these essential conditions:
>
> ℞ Iron sulfate ℥ss
> Potassium subcarbonate ℥ss
>
> Pulverize separately, mix slowly and carefully, then add:
>
> Tragacanth mucilage q.s.
>
> Pound up vigorously and make a mass; divide into 48 pills.

The dosage was two pills daily for three days; three pills daily for three days; four pills daily for

three days; thereafter, twelve pills daily until well. Each pill contained 5 gr. (0.3 gm.) of iron sulfate; twelve contained 60 gr. (4 gm.), a daily dose which compares favorably with that recommended by the most recent advocates of large doses of iron in secondary anemia.

He reported thirty cases.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPSIS FOLLOWING CESAREAN SECTION FOR PARTIAL SEPARATION OF THE PLACENTA

Mrs. E., a thirty-three-year-old primipara at term, was sent into the hospital for the purpose of induction on October 27, 1932. Before this was done, the patient had soaked two pads with bright-red blood and passed some clots.

The family history was non-contributory. The patient had had scarlet fever and measles as a child; the appendix had been removed in 1920, and the operation had been followed by pneumonia. The tonsils had been taken out twice, and the patient had had arthritis in the hands. Curettage and cervical dilatation for sterility had been performed in 1931. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five days. The last period began January 17, making the expected date of confinement October 24. The pregnancy had been uneventful.

At entry, the uterus was not relaxed and the fetal heart was heard. It was evident that she had a partial separation of the placenta, and a cesarean was decided upon. This was performed under nitrous oxide, oxygen and ether anesthesia, and a male child, weighing 8 pounds, 1 ounce, was delivered in good condition.

On October 28, the day following the operation, the afternoon temperature was 102°F. and rose during the evening to 104. The next afternoon it went to 105°F. following a chill. On October 30 the morning temperature was 103°F., and the pulse 120. The abdomen was soft, and there was some distention. A medical consultation revealed nothing in the chest. The patient ran an irregular temperature for ten days, ranging from 100 to 104°F. in the afternoon. During this time she drained large amounts of thick, foul-smelling lochia. The abdomen was negative, and there was no nausea or vomiting. Although no cultures were taken from the uterus, she undoubtedly had uterine sepsis. Toward the end of the infection a mass developed on the left, almost at the level of the anterior superior spine. She was discharged on November 16, completely well.

When seen on December 8, the mass had entirely disappeared.

Comment. This is a case of uncomplicated uterine sepsis following a clean cesarean section. There was no evidence of peritonitis at the time of operation. The etiology of the infection is unknown as no blood or uterine cultures were taken. The treatment was entirely conservative: the uterus was left alone, and only supportive treatment was administered.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

TREASURER'S REPORT

COVERING REFUND DISTRIBUTION

The Treasurer of the Massachusetts Medical Society makes the following report regarding the refund to the district societies for 1940.

The Council voted to distribute the sum of $5000 to district societies. The total number of payments of annual dues received by the Treasurer by March 4, to be counted for the refund, was 4058. Therefore the refund to the district societies for each paid fellow is $1.232.

The following table gives the number of payments in, and the refund to, each district, as of March 26:

DISTRICT	NUMBER REPORTED PAID	REFUND
Barnstable	47	58.00
Berkshire	109	134.29
Bristol North	56	69.10
Bristol South	159	195.89
Essex North	175	215.60
Essex South	223	274.74
Franklin	39	48.18
Hampden	296	364.67
Hampshire	57	70.32
Middlesex East	109	134.29
Middlesex North	113	139.22
Middlesex South	813	1001.62
Norfolk	721	888.27
Norfolk South	107	131.82
Plymouth	115	141.68
Suffolk	500	616.00
Worcester	341	420.11
Worcester North	78	96.20
	4058	$5000.00

In 1939, for comparison, the total number of payments for the refund was 3916.

CHARLES S. BUTLER, M.D., *Treasurer.*

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning April 7:

BERKSHIRE

Thursday, April 11, at 4:30 p.m., at the Bishop House of Mercy Hospital, Pittsfield. Complications in Obstetrics: Illustrated by case histories. Instructor: Robert L. DeNormandie. Harry G. Mellen, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, April 9, at 4:30 p.m., at the Union Hospital, Fall River. Head and Spine Injuries. Instructor: Walter R. Wegner. Howard P. Sawyer, *Chairman.*

FRANKLIN

Thursday, April 11, at 8:15 p.m., at the Franklin County Hospital, Greenfield. Head and Spine Injuries. Instructor: Donald Munro. Halbert G. Stetson, *Chairman.*

HAMPDEN

Thursday, April 11, at 4:00 p.m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:15 p.m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Gonorrhea in the Female. Instructor: Oscar F. Cox, Jr. George L. Schadt, *Chairman.*

HAMPSHIRE

Thursday, April 11, at 4:15 p.m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Cardiovascular Disease: Eleven important questions about heart disease and their answers. Instructor: R. Earle Glendy. Warren P. Cordes, *Chairman.*

MIDDLESEX SOUTH

Tuesday, April 9, at 4:30 p.m., at the Cambridge Hospital, 330 Mt. Auburn Street, Cambridge. Common Problems of Neurology: Indications for lumbar puncture. Instructor: H. Houston Merritt. Dudley Merrill, *Chairman.*

NORFOLK

Thursday, April 11, at 8:30 p.m., at the Norwood Hospital, Norwood. Common Problems of Neurology: Indications for lumbar puncture. Instructor: H. Houston Merritt. Hugo B. C. Riemer, *Chairman.*

NORFOLK SOUTH

Monday, April 8, at 8:30 p.m., at the Quincy City Hospital, Quincy. Convulsions in Infants and Children: Etiology and treatment. Instructor: R. Cannon Eley. David L. Belding, *Chairman.*

PLYMOUTH

Tuesday, April 9, at 4:00 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Indications for Cesarean Section. Instructor: Raymond S. Titus. Walter H. Pulsifer, *Chairman.*

SUFFOLK

Thursday, April 11, at 4:30 p.m., in John Ware Hall, Boston Medical Library, 8 Fenway, Boston. Pneumonia. Instructor: Maxwell Finland. Reginald Fitz, *Chairman.*

DEATHS

BAILEY — GEORGE G. BAILEY, M.D., of Ipswich, died March 30. He was in his seventy-sixth year.

He received his degree from the Harvard Medical School in 1892. Dr. Bailey was a fellow of the Massachusetts Medical Society and the American Medical Association and was a member of the staff of the Cable Memorial Hospital, Ipswich. He had recently resigned his position as medical examiner, which he had held for forty-two years, because of ill health.

His widow, a son, Dr. George G., Jr., and two daughters survive him.

MARSHALL — AUGUSTUS T. MARSHALL, M.D., of Randolph, Vermont, died recently. He was in his sixty-fifth year.

Dr. Marshall received his degree from Dartmouth Medical School in 1901 and was a fellow of the Massachusetts Medical Society and the American Medical Association.

SMITH — FORSTER H. SMITH, M.D., of Lowell, died recently. He was in his sixty-fourth year.

Dr. Smith received his degree in 1902 from the Harvard Medical School. He was former superintendent of the Lowell Isolation Hospital, and a former member of the Massachusetts Medical Society.

His widow and a son survive him.

MISCELLANY

MAINE NEWS

REMOVAL NOTICES

The following removal notices have been received:

George W. R. Bowie, M.D., from New Gloucester to Vanceboro.

E. Allen McLean, M.D., from 201 State Street, to 29 Deering Street, Portland.

MAINE MEDICAL ASSOCIATION

The following physicians have been recently admitted to membership in the Maine Medical Association:

Ernest L. Coffin, M.D., Northeast Harbor.
Henry Almond, M.D., Gardiner.
Wilfred J. Comeau, M.D., Bangor.
Paul A. Millington, M.D., Newport.
John Valentine, M.D., Dover-Foxcroft.
Willis B. Mitchell, M.D., Wiscasset.

CORRESPONDENCE

AUSTEN FOX RIGGS

To the Editor: In the *Journal* of March 14, 1940, the death of Austen Fox Riggs of Stockbridge was announced.

I should like to take this opportunity of paying tribute to a physician whose professional career was as striking as the gallant conduct of his life. Dr. Riggs had pre-

pared himself for the practice of internal medicine and had been assistant to Dr. Walter B. James, of New York City, for three years when conditions of health made it advisable for him to leave New York City and to take up residence in the Berkshires. There for over thirty years, and frequently despite personal ill health, he devoted himself to his chosen field of work — the treatment of nervous patients burdened with personal difficulties, unable to deal unaided with problems of life. In this task he was peculiarly successful; he gathered around him a group of able young associates, he kept abreast of medical progress, and he considered earnestly the objective appraisal of his work by his medical colleagues. Not satisfied with the mere exercise of his professional skill, he carefully analyzed methods and results in the attempt to formulate general principles. Before his death he had the satisfaction of seeing in manuscript form a critical statistical analysis of his life work. Dr. Riggs emphasized the value of his chosen psychotherapeutic methods, and was somewhat impatient with the suggestion that his results depended more on his unusual personal influence than on the special methods he employed. His patients could not but be influenced by his sincerity, sympathy and optimism and by his imposing presence.

As a consultant he was held in high value by colleagues and hospitals. His many interests were indicated by the large number of organizations with which he was affiliated. He inspired a deep affection among an unusual number of friends.

The medical profession has lost a member of unusual valuc, the community a wise adviser, and he leaves his widow and four children a precious memory.

C. Macfie Campbell.

74 Fenwood Road
Boston.

DONATIONS OF BOOKS AND PERIODICALS

To the Editor: I have had urgent requests for books and periodicals from both China, where the disruption of hospitals and medical schools has made difficult the securing of medical literature, and also from refugees in Mexico who have wholly lost their libraries and their contact with recent literature. If readers of this note should have spare copies of books or periodicals which they would be willing to contribute to either China or Mexico, may I ask that they send them to Miss Anna C. Holt, Librarian, Building A, Harvard Medical School. If donors prefer that their gifts be sent to one country or the other, they should indicate their preference.

Walter B. Cannon.

25 Shattuck Street,
Boston, Mass.

REPORT OF MEETING

GREATER BOSTON MEDICAL SOCIETY

A regular meeting of the Greater Boston Medical Society was held on January 2, at the Beth Israel Hospital. Dr. Max Ritvo introduced Dr. Abraham Myerson, who spoke on "Recent Advances in the Treatment of Epilepsy and Schizophrenia."

Dr. Myerson explained that these two seemingly diverse conditions were being considered together because of the suggestive similarity in brain waves and because schizophrenia has recently been treated by the induction of epileptiform convulsions.

The first consideration was epilepsy, which was defined as a periodic loss or impairment of consciousness, with or without associated convulsions. In the grand-mal type of seizure there are convulsions, whereas the attacks of petit mal merely result in temporary unconsciousness. An additional type of epilepsy, called by Gibbs and Lennox the "psychomotor attack," is characterized by organized motions in the unconscious state.

The speaker cited various factors which appear to influence the incidence of attacks in a susceptible person. Their occurrence during sleep, as well as during the periods of falling asleep and awakening, has long been observed and has more recently been related to the similarity of the electroencephalographic tracings of the sleeping person and epileptic. The incidence of seizures during organic disease of the central nervous system is greater than can be expected by chance. The fact that drugs such as Metrazol induce convulsions has been the basis of the recent shock treatment of schizophrenia. Hyperventilation, and indeed alkalosis of any sort, favors the onset of attacks, and the favorable effects of acidosis were the basis of the formerly employed ketogenic diet in the treatment of epilepsy. Further studies serve to indicate that cerebral dehydration and an elevated blood sugar are also beneficial in this condition.

One of the great advances in the study of the mechanism of epilepsy was the introduction by Berger in 1929 of the electroencephalogram, which has subsequently been elaborated and its findings extensively interpreted by Lennox and Gibbs. The latter workers have insisted on the recognition of the underlying "paroxysmal cerebral dysrhythmia." They maintain that epilepsy is in reality a chronic disorder with clinical manifestations, other than the abnormal electroencephalogram, observed only during periodic "explosions." Similar tracings during sleep show bursts of activity very suggestive of epilepsy, and the resemblance of these cerebral dysrhythmias to those of the respiratory system was suggested by Dr. Myerson. Clinical evidence and brain-wave tracings corroborate the fact that voluntary effort, either mental or physical, aids in warding off an incipient epileptiform seizure — a fact that most patients soon learn empirically.

Dr. Myerson showed typical electroencephalographic charts of Lennox and Gibbs, which demonstrated the increasing frequency and irregularity of waves during a grand-mal seizure, and the characteristic wave and spike of the petit-mal attack, coming in bursts in both instances, even in the absence of clinical signs or symptoms. The findings during a psychomotor attack were not considered so constant by Dr. Myerson. Characteristically, there is a slow plateau type of wave, which Lennox and Gibbs have found very similar to some tracings in schizophrenic patients. Another well-known observation resulting from the extensive use of electroencephalograms by Gibbs and Lennox was the greater incidence of pathologic wave tracings in relatives of epileptic patients than in the population at large, but no exact correlation has been proved to exist between abnormal waves and clinical manifestations of epilepsy.

Dr. Myerson concluded his discussion of epilepsy with a résumé of the development of therapy and an appraisal of its present status. Sedatives had long ago proved their efficacy, but the bromides, which were first used, produced toxic symptoms when employed in sufficient quantities to minimize the convulsions. Phenobarbital was then used with commendable results, particularly in relatively large doses for grand-mal seizures. Then the researches of Putnam and Merritt showed the phenyl group to be the important constituent of the barbiturates and resulted in the

introduction of the new drug, Dilantin (diphenyl hydantoin). This is largely free of the unpleasant and occasionally dangerous sedative effects of the barbiturates and has proved at least promising in therapy. For the past three years, Dr. Myerson and his collaborators have endeavored to assay the value of various therapeutic agents in the treatment of 150 patients at the Grafton State Hospital. One group has received greatly increased doses of the barbiturates, with stimulants when necessary to allay the sedative effects. Another group received Dilantin, a third group Dilantin and ordinary doses of phenobarbital, while the last group received another new drug, Meborol. The first group showed 65 per cent decrease in number of seizures, while the third group had a reduction of 85 per cent, with the greatest value being exhibited in the grand-mal type of seizure. The two newer drugs alone, on the other hand, showed their greatest effect in the petit-mal and psychomotor attacks and were much less prone to cause depressing toxic effects. On the whole, Dr. Myerson concluded that the prognosis for epilepsy was now far from hopeless.

The speaker then continued with a discussion of schizophrenia, pointing out that this condition is now known to have an acute form and may exhibit spontaneous reversals, so that it is not necessarily a chronic and hopeless disease as formerly believed. The facts that Amytal and amphetamine have been demonstrated to cause a temporary remission and that insulin and Metrazol therapy have "produced" remissions of longer or shorter duration serve to indicate that drug therapy may eventually solve the problem. The results so far, however, have failed to attain the success originally predicted.

Dr. Myerson described his "total push" method for helping these unfortunate patients. This was based on the concept that these patients were not aided but rather hindered by the superimposition of a prison psychosis on their fundamental imbalance. Therefore it was decided to interest the patients in physical and mental exercises and to offer praise or blame, reward or punishment, where it was merited. The patients chosen were those who had been sick for over ten years and who had had no remissions. These people have now been treated for more than a year, and although no claims can be made for cures, several patients have improved sufficiently to be released from the institution, for all or part of the time. It was concluded, therefore, that the main problem at present in treating schizophrenia in the absence of a specific drug was to abolish defeatism among the medical profession.

The discussion was inaugurated by Dr. William G. Lennox, who stated that the incidence of abnormal electroencephalograms among essentially normal persons as well as among asymptomatic relatives of epileptic patients had put emphasis on the significance of the fundamental dysrhythmia rather than on the occurrence of seizures. Ten per cent of supposedly normal people exhibit persistent changes in their brain waves, while the incidence in relatives of epileptics is eight times normal. The problem, then, is to determine who are going to have symptomatic manifestations. Dr. Lennox stated that there is probably a change of the arterial carbon dioxide content to an elevated level in grand-mal and to a lowered level in petit-mal seizures. The results with Dilantin at the Boston City Hospital have not been so good in petit-mal attacks as have been those of Dr. Myerson, and it was believed that this was the result of better diagnosis which put some of these cases in their true category of psychomotor disturbances where this drug is particularly efficacious.

Dr. H. Houston Merritt discussed, with diagrams, the rationale of the development of the newer phenyl derivatives and expressed the hope that a truly specific drug might be forthcoming.

Dr. Kenneth J. Tillotson emphasized the value of the electroencephalogram in mental institutions, particularly in regard to schizophrenia. At the McLean Hospital, 2 of the 11 worst schizoid patients chosen for Dr. Myerson's total-push method have left the hospital, while 8 of the remaining 9 have shown tremendous improvement. Of a total of 75 persons so treated, some following unsuccessful shock therapy, many have left the hospital and the majority have shown immeasurable gain.

Dr. Harry C. Solomon mentioned the American method of treating schizophrenic patients as psychologic rather than as organic problems, but said that there probably was some of each factor playing a role. Although the incidence of abnormal electroencephalographic findings is higher in these people than in the population at large, the fact that some ostensibly normal individuals have more abnormal findings than do many schizoid patients makes any conclusions as to the nature of the condition uncertain. The speaker warned that in the appraisal of drug therapy, one should always be cognizant of the 20 to 30 per cent of spontaneous cures with little or no residual damage. Dr. Solomon concluded by lauding the total-push system for enabling schizophrenia to be studied without any complicating institutional psychosis and for awakening the profession to the possibilities of treatment in this disease.

Dr. Wilfred Bloomberg stated that the original definition of schizophrenia included a hopeless prognosis and that cures made the diagnosis untenable. He has observed in prisons that long-term inmates often develop a condition surprisingly similar to a simple schizophrenia, where they prefer to return to the seclusion of Charlestown State Prison rather than to remain at the Norfolk Farm, where forward-looking criminologists attempt a regimen like that of Dr. Myerson. Dr. Bloomberg was of the opinion that some schizoid patients, therefore, are better off in seclusion than they are in being brought to face what they have been fleeing.

NOTICES

BOSTON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday, April 10, at 12 o'clock noon, in the Pathological Amphitheater.

BOSTON LYING-IN HOSPITAL

The Journal Club will hold its next meeting in the lecture hall of the Boston Lying-in Hospital on Tuesday, April 16, at 8:15 p.m. Dr. Abraham Myerson will discuss "The Heredity of Mental and Nervous Disease and Eugenical Sterilization."

Physicians and students are cordially invited to attend.

HOSPITAL COUNCIL OF BOSTON

The annual meeting of the Hospital Council of Boston will be held at the New England Deaconess Hospital on Tuesday, April 9, at 12:30 noon. Action will be taken on the applications of the Boston Lying-in Hospital and the Cambridge Hospital for membership.

PROGRAM

Convalescence and the Nursing-Home Information Bureau. Miss Carrie M. Hall.

Mr. Frank E. Wing will report on the following:

Should the New England Hospital for Women and Children Increase its Obstetrical Facilities?

Is There Need for Outpatient Facilities at the New England Baptist Hospital?

City Responsibility for Reimbursement for Care of Relief Clients in Voluntary Hospitals.
Salaries.
Legislation. Dr. Charles F. Wilinsky.

Members of the medical profession are cordially invited to attend. The charge for luncheon will be 75 cents. Reservations should be made before April 6 (LIB 8515).

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The first concert of the Boston Doctors' Symphony Orchestra, Alexander Thiede, conductor, will be held at 8:15 on Sunday evening, May 5, at Jordan Hall. Tickets are priced at one dollar, and the proceeds will be given to a medical charity. The ticket committee is composed of Dr. Welman B. Christie, chairman, 15 Bay State Road, Boston, Dr. Julius Loman, 1284 Beacon Street, Brookline, and Dr. Robert G. Vance, 262 Beacon Street, Boston.

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, April 16, at 12 o'clock noon. Dr. Edward D. Churchill will speak on "Surgery of the Lungs."

Physicians are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A research conference of the medical staff of the Peter Bent Brigham Hospital will be held in the amphitheater of the hospital on Tuesday, April 9, at 5:00 p.m.

PROGRAM

Experiments with the Miller Abbott Tube and Chemistry of the Jejunal Juices. Drs. Lemuel C. McGee and E. S. Emery, Jr.
Observations on the Effect of Salyrgan on Blood Volume. Dr. Reginald Fitz.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, April 10, from 2 to 4 p.m. Drs. E. C. Cutler and Soma Weiss will speak on "The Unconscious Patient."

Physicians and students are cordially invited to attend.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, April 9, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance), at 8:15 p.m. Dr. Soma Weiss will preside.

PROGRAM

Experimental Observations on the Physiology of Shock. Dr. John G. Gibson, 2nd.
Observations on the Pathology of Shock. Dr. John E. Dunphy.
Clinical Aspects of Shock. Dr. Eugene A. Stead, Jr.

Medical students and physicians are cordially invited to attend.

SIR WILLIAM OSLER HONORARY SOCIETY

The annual lecture of the Sir William Osler Honorary Society of the Tufts College Medical School will be given by Dr. Chester S. Keefer on Friday evening, April 26, at 8:00, in the Beth Israel Hospital Auditorium, Boston.

Dr. Keefer will speak on "The Clinical Interpretation of Bacteremia."

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

SCHOOL INSPECTOR, BOARD OF HEALTH, $600 A YEAR, EVERETT

Director of State Civil Service, Ulysses J. Lupien, has announced that competitive examinations are to be held on April 26 in order to find eligibles for appointment to the position of School Inspector, Board of Health, Everett.

The entrance requirement is as follows: applicants must be registered physicians under the State Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Friday, April 12, at 5:00 p.m.

MEDICAL INSPECTOR (MALE) $700 A YEAR, SPRINGFIELD

Director of State Civil Service, Ulysses J. Lupien, has announced that competitive examinations are to be held on May 4 in order to find eligibles for appointment to the above position.

The entrance requirement is as follows: applicants must be registered physicians under the State Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Saturday, April 20, at 12 o'clock noon.

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held at the Peter Bent Brigham Hospital on Thursday, April 18, at 8:00 p.m. Dr. Hamilton Montgomery, a member of the Section on Dermatology, Mayo Clinic, will speak on the subject "Pathologic Features of Some of the Non-neoplastic Dermatoses."

Physicians and medical students are cordially invited.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The annual meeting of the New England Dermatological Society will be held on Wednesday, April 10, at 2:00 p.m., at the Boston City Hospital. At 5:00 p.m., Dr. Alan R. Moritz will speak on "Accident, Murder or Suicide?" Following the meeting, dinner and entertainment will be held at the Hotel Kenmore.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The regular spring meeting of the New England Oto-Laryngological Society will be held at the Massachusetts

Eye and Ear Infirmary, 243 Charles Street, Boston, on Wednesday, April 10, at 4:00 p.m.

PROGRAM

4:00 p.m. Presentation of hospital cases. Dr. LeRoy A. Schall and infirmary staff.
Acute Surgical Mastoiditis Following Fracture of the Skull. Dr. Herman Winkler, Providence, Rhode Island.
Bronchial Asthma Due to Bacterial Allergy. Dr. Warren Kershner, Bath, Maine.
Osteomyelitis of the Frontal Bone. Dr. Adolphe Provost, Manchester, New Hampshire.
Complications of a Parapharyngeal Abscess. Dr. Louis M. Freedman.
Preventing the Chronic Running Ear. Dr. Harry Goodspeed, Worcester, Massachusetts.
6:30 p.m. Buffet supper.
7:45 p.m. Business meeting.
8:00 p.m. Chemotherapy of Otitis Media. Dr. Champ Lyons. Discussion: Drs. Robert N. Ganz and Carl H. Ernlund.

NEW ENGLAND INSTITUTE OF HEALTH

The New England Health Institute will be held in Hartford, Connecticut, the entire week of April 15–19. The headquarters and all lectures will be at Hotel Bond, 320 Asylum Street. Registration will begin Monday morning, April 15, at nine o'clock and will continue through the week. A fee of one dollar will be charged to cover routine expenses.

The lectures will begin at 2 p.m., Monday afternoon, and four lectures will be given simultaneously each hour, from 9:30–12:30, and from 2:00–5:00. Signals will be given five minutes before each hour so that each lecture will close promptly and the next lecture begin on time. Lectures are open to all those who are interested in public health or actively engaged in the work. The various sections and chairmen are as follows:

SECTION	CHAIRMEN
Public-Health Administration	John A. Ferrell, M.D.
Preventable Diseases	Wilson G. Smillie, M.D.
Sanitary Engineering	Roscoe H. Suttie, C.E.
Vital Statistics	Halbert L. Dunn, M.D.
Laboratory	Elliott S. Robinson, M.D.
Venereal Diseases	R. A. Vonderlehr, M.D.
Industrial Hygiene	R. R. Sayers, M.D.
Cancer	C. L. Larkin, M.D.
Tuberculosis	David R. Lyman, M.D.
Child Hygiene	Martha M. Eliot, M.D.
Crippled Children	R. C. Hood, M.D.
Nutrition	George R. Cowgill, Ph.D.
Public-Health Nursing	Mary D. Forbes, R.N.
Mental Hygiene	Eugene Kahn, M.D.
Health Education	Clair E. Turner, Dr.P.H.
Milk, Food and Drugs	E. G. Woodward, A.M.

On the evening of Tuesday, April 16, a dinner for the faculty of the Institute will be held at Hotel Bond. A minimum charge will be made for this event. This will be the high spot in the program.

Health moving pictures will be shown daily from 5:00–6:00.

Those desiring detailed information should apply to the State Department of Health, Hartford, Connecticut.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted at Atlantic City, New Jersey, from Friday, June 7, through Monday, June 10, prior to the opening of the annual meeting of the American Medical Association in New York City on Wednesday, June 12. Formal notice of the exact time and place of the examination will be forwarded to each candidate several weeks in advance of the examination dates. Group A candidates will be examined on June 7 and 8, and Group B candidates on June 9 and 10.

Candidates for re-examination in Part II must make written application to the Secretary's Office before April 15.

The annual dinner of the board will be held in New York City on Wednesday evening, June 12, at the Hotel McAlpin. Diplomates certified at the preceding days' examinations will be introduced personally, and there will be several speakers. All diplomates of the board, and others interested in the work of the board, are cordially invited to attend this dinner.

Tickets at $3.50 each may be obtained from Dr. Joseph L. Baer, chairman, 104 S. Michigan Avenue, Chicago, Illinois, or at the registration desk during the examinations.

For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, APRIL 7

TUESDAY, APRIL 9

*9–10 a.m. Studies on Purpura in Relation to the Spleen and Bone Marrow. Dr. William Dameshek. Joseph H. Pratt Diagnostic Hospital.
*12:30 p.m. Hospital Council of Boston. New England Deaconess Hospital.
5 p.m. Research conference of the medical staff, Peter Bent Brigham Hospital amphitheater.
*8:15 p.m. Harvard Medical Society. Peter Bent Brigham Hospital (Shattuck Street entrance).

WEDNESDAY, APRIL 10

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
12 m. Monthly clinicopathological conference. Boston City Hospital, Pathological amphitheater.
2 p.m. New England Dermatological Society. Boston City Hospital.
*2–4 p.m. The Unconscious Patient. Drs. E. C. Cutler and Soma Weiss. Peter Bent Brigham Hospital.
4–8 p.m. New England Oto-Laryngological Society. Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston.

THURSDAY, APRIL 11

*9–10 a.m. Diagnostic Errors. Dr. H. G. Brugsch. Joseph H. Pratt Diagnostic Hospital.

FRIDAY, APRIL 12

*9–10 a.m. Prothrombin and Vitamin K. Dr. E. L. Lozner. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, APRIL 13

*9–10 a.m. Hospital case presentation. Dr. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

APRIL 5 — William Harvey Society. Page 561, issue of March 28.

APRIL 5 — Chelsea Naval Hospital. Page 561, issue of March 28.

APRIL 11 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

APRIL 15–17 — American Association for the Study of Goiter. Page 203, issue of February 1.

APRIL 15–19 — New England Health Institute. Page 284, issue of February 15, and notice above.

APRIL 16 — Journal Club meeting. Boston Lying-in Hospital. Page 606.

APRIL 16 — South End Medical Club. Page 607.

APRIL 18 — New England Pathological Society. Page 607.

APRIL 24 — Massachusetts Dental Society. Page 365, issue of February 29.

APRIL 24–26 — Scientific Session. Academy of Physical Medicine. Hotel John Marshall, Richmond, Virginia.

APRIL 26 — Sir William Osler Honorary Society of the Tufts College Medical School. Page 607.

MAY 10–18 — American Scientific Congress. Page 1043, issue of December 28.

MAY 13 — United States Pharmacopoeial Convention. Page 202, issue of February 1.

JUNE 7–8 — American Heart Association. Page 469, issue of March 14.

JUNE 7–10 — American Board of Obstetrics and Gynecology. Page 608.

JUNE 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

JUNE 10–14 — American Physicians' Art Association. Page 332, issue of February 22.

JUNE 23-25 — Maine Medical Association. Annual meeting. Rangeley Lakes.

OCTOBER 21 — American Board of Internal Medicine, Inc. Page 369, issue of February 29.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

MAY 8 — Annual meeting. Salem Country Club, Peabody.

FRANKLIN

MAY 14 — Franklin County Hospital, Greenfield.

HAMPSHIRE

MAY 8, at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

MAY 15, at 12:15 p.m. at the Unicorn Country Club, Stoneham.

MIDDLESEX NORTH

APRIL 24.

JULY 31.

OCTOBER 30.

NORFOLK SOUTH

MAY 2.

PLYMOUTH

APRIL 18 — State Farm.

MAY 16 — Lakeville State Sanatorium, Middleboro.

SUFFOLK

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

MAY 2 — Censors' meeting. Page 244, issue of February 8.

WORCESTER

APRIL 10 — Worcester Hahnemann Hospital.

MAY 8 — Worcester Country Club.

Meetings begin with a dinner at 6:30 p.m. and are followed by a business and scientific meeting.

BOOK REVIEWS

Synopsis of Pediatrics. John Zahorsky and T. S. Zahorsky. Third edition. 430 pp. St. Louis: C. V. Mosby Co., 1939. $4.00.

To compress the whole of pediatrics — feeding, growth and hygiene, as well as diseases — into a pocket-size volume of 400 pages is no easy task, but the Drs. Zahorsky have succeeded in so doing. Naturally the consideration of particular matters is brought down to the irreducible minimum, but the information furnished, though skeletonized, covers all the essential ground. The book is conservative in tone but has been brought entirely up to date. The mere fact that it has passed through three editions in something like six years is proof that it is serving a useful purpose. It should, however, be of more use to the practitioner to whom pediatrics is only an incidental part of practice; the pediatrician has or ought to have most of its material at his fingertips. It may also be recommended to the medical student who wishes to check up or refresh his memory. As books go, it is of excellent value.

Facts and Theories of Psychoanalysis. Ives Hendrick. Second edition. 369 pp. New York: Alfred A. Knopf, 1939. $3.00.

As this excellent survey brings up to date all the new developments in psychoanalysis, it is a source of satisfaction that it has now gone into a second revised and enlarged edition. It fulfills the demand due to the increased interest in the scientific aspects of psychoanalysis by psychiatrists and the general medical profession. The book is a basic one and provides an accurate text for a sound understanding of psychoanalysis. The author correctly emphasizes that, in the five years that have elapsed since the appearance of the first edition, there have been no discoveries which have refuted the basic theoretical and practical principles of psychoanalysis.

The volume is divided into four sections: the basic facts of analysis; its theories; analytic therapy; and the various medical and other professional applications of the psychoanalytic movement. Among the additions to this revised edition are a discussion of the psychology of female sexuality, recent data on the therapeutic results of psychoanalysis from the Berlin, London and Chicago institutes, an amplification of the previous brief discussion on child analysis, an extended consideration on the psychology of organic disease (psychosomatic reactions), the cultural aspects of psychoanalysis, sections on the systematic training of psychoanalysts as carried out by the various training institutes, suggestions for further reading and a fairly complete glossary of psychoanalytic terms.

There are several features of the volume to which the reviewer would like to call particular attention. The first of these is an account of the two-year investigation of psychoanalysis by a special committee of the British Medical Association, subsequently published in the *British Medical Journal*. This special committee concluded that the term "psychoanalysis" can be applied only to the methods and theories evolved by Freud. The section on the recent therapeutic results of psychoanalysis already referred to is of particular interest to the medical profession. Several features are pointed out with which analysts and analytically trained psychiatrists would agree. For instance, cures of symptoms alone are never regarded as significant, the goal of analytic therapy being an adjustment to the problems of life, an adequate strengthening in handling the crippling and suffering symptoms of a neurosis and an increase in capacity of the patient's potentialities.

On the whole, the volume epitomizes the science of psychoanalysis as it is understood today and is therefore of decided value to students, social workers, physicians and psychiatrists.

Psychopathia Sexualis: A medico-forensic study. Richard von Krafft-Ebing. Twelfth edition. 626 pp. New York: Pioneer Publications, Inc., 1939. $3.00.

This is an inexpensive edition of a standard work on sexual pathology. It is an English translation from the twelfth German edition of 1903, and this translation was first published in 1906. It is now reissued with an introduction and an appendix by Victor Robinson of New York City. The appendix of a little more than eight pages briefly discusses psychoanalysis, endocrinology and the discovery of hormones by Bayliss and Starling, and the censorship of sexual literature by the federal authorities. Krafft-Ebing was a pioneer in the field of sexual

pathology and his work went through seventeen editions, the last being issued in Stuttgart in 1924. However, the twelfth edition was the last published from his own manuscript, as he died in 1902, and that edition should be recognized as the authoritative text embodying his latest ideas.

A Textbook of Pathology for Nurses. Coleman B. Rabin. Second edition, revised. 260 pp. Philadelphia and London: W. B. Saunders Co., 1939. $1.75.

If we admit that it is desirable for nurses to be subjected to a rather detailed course in pathology and clinical pathology, and if we assume that a good purpose justifies simplification of pathological conceptions, then Dr. Rabin has succeeded admirably in fulfilling his purpose. This book follows the plan laid down for the course in pathology given to the students of the Mount Sinai Hospital School of Nursing of New York City. Through twenty-two chapters devoted to pathology the author lays emphasis on the mechanism of disease processes and the correlation of diseased structure with diseased function. Consideration is given the degenerative and inflammatory changes in the body, with special attention to the more important infections, such as tuberculosis and typhoid fever. There is one chapter on ulcers and another on neoplasms. Five chapters are devoted to a consideration of the consequences of obstruction to the viscera. The author has used to good advantage the method originated by MacCallum in the presentation of his material. Four brief well-arranged chapters are devoted to clinical pathology. The rather large number of illustrations has been well chosen. In addition diagrammatic representations do much to augment the text.

On the whole the author has not departed from facts in his attempt to simplify the subject. This book should serve as an excellent text for a course in pathology in a nurses' training school.

The Treatment of Rheumatism in General Practice. W. S. C. Copeman. Third edition. 276 pp. Baltimore: The Williams & Wilkins Co., 1939. $4.00.

The fact that this book is now in its third edition indicates an appeal which your reviewer fails to appreciate. The book is full of traditions, both for diagnosis and treatment, but there is little substantiation. The best explanation for its appeal is that it contains many recommendations for treatment which can be carried out by the general practitioner, though here in New England we should doubt their value. The use of vaccines is recommended, but not justified. Most drugs, except aspirin, are damned with faint praise. Colchicine is not mentioned in the treatment of gout. Atophan and antipyrine are advised, with no mention of their toxicity. Intestinal antiseptics are not recommended; diets are not so simple as they are in the United States; stress is laid on the need of an alkaline-ash diet, colonic lavage and medication baths, and spa treatments are given too much prominence. The value of treatment by orthopedists is slighted.

A Textbook of Obstetrics: With special reference to nursing care. Charles B. Reed and Bess I. Cooley. 476 pp. St. Louis: The C. V. Mosby Co., 1939. $3.00.

For a book which is described as being "brand new," this textbook of obstetrics can hardly be said to be an improvement over the books already published.

The first few chapters, describing anatomy, physiology and embryology, together with that on prenatal care in the normal pregnant woman, are satisfactory. In connection with many of the complications of pregnancy, however, there are to be found gross errors of commission and omission. In addition, the reviewer could not help noticing many ambiguous statements in which the wording makes the text very difficult to understand. There are many mistakes in spelling throughout the book and these, together with at least one inverted illustration, lead one to infer that the proofreading has been very carelessly done. Consequently, it is difficult to recommend this book.

Teaching for Health. Marguerite M. Hussey. Second edition. 328 pp. New York: Prentice-Hall, Inc., 1939. $2.25.

Miss Hussey is assistant professor of education at New York University, and her work on the relation of teaching to health has required a second edition within a year of its first publication. The book is written from the point of view of the teacher and discusses the factors affecting health which are directly or indirectly controllable by the teacher. Of special interest are the chapters on the relations of the home and parents with the school in the promoting of child health. Under printed materials, standards are set up for evaluating hygienic textbooks. Although the book is primarily a technical manual of methods for promoting the health of the child by the schools, it should prove useful to school physicians and nurses in giving the views of those interested in this type of education.

A Topographic Atlas for X-Ray Therapy. Ira I. Kaplan and Sidney Rubenfeld. 120 pp. Chicago: The Year Book Publishers, Inc., 1939. $4.00.

This quarto volume consists of fifty-five plates, 5¾ by 7 inches in size. On the page facing each plate is a concise explanation. The information given by illustrations and text can, of course, be culled from works on topographical anatomy, especially works on surface projections. This volume may serve as a short cut for radiologists or as a guide to technicians. Superficiality is the fellow traveler on all short cuts to fundamental knowledge; this work carries that stigma.

Manual for Diabetic Patients. W. D. Sansum, Alfred E. Koehler and Ruth Bowden. 227 pp. New York: The Macmillan Co., 1939. $3.25.

The discussion of the nature, diagnosis and dietary treatment of diabetes in this manual is adequate but better suited to the physician than to the patient. In view of the authors' early recommendation of diets containing more liberal quantities of carbohydrate than had previously been used, one naturally turns to their present practice and learns "that we are feeding our adult diabetic patients from 150 to 300 grams and our diabetic children from 100 to 400 grams of carbohydrate daily." Various common complications of diabetes are described and preventive measures recommended. In addition to testing the urine for sugar, it is considered desirable that the patient know how to make the tests for acetone and diacetic acid.

Erratum

In the listing of the book review, *Surgical Applied Anatomy,* by Frederick Treves (*New Eng. J. Med. 222:* 334, 1940), the price was given as $4.00; it should have read $4.50.